Archives of Dermatology and Syphilology

VOLUME 38 AUGUST 1938 NUMBER 2

COPYRIGHT, 1938, BY THE AMERICAN MEDICAL ASSOCIATION

LXXX.—BLASTOMYCOSIS, COCCIDIOIDAL GRANULOMA AND PARACOCCIDIOIDAL GRANULOMA

COMPARATIVE STUDY OF NORTH AMERICAN, SOUTH AMERICAN AND EUROPEAN ORGANISMS AND CLINICAL TYPES

MORRIS MOORE, PH.D.

Mycologist to the Barnard Free Skin and Cancer Hospital, the Barnes Hospital and the Washington University School of Medicine

ST. LOUIS

The term blastomycosis in its medical interpretation has come to denote a more or less definite clinical syndrome with a multiplicity of causative agents. The disease has been so named because of the finding in the affected tissue or pus of budding yeastlike cells which are ordinarily termed blastomycetes—hence, blastomycosis. This is particularly evident to readers of dermatologic publications, since the skin as a tissue is the recipient of approximately 95 per cent of infections by these organisms. Impetus has been given to publications on this disease by the increased interest in the action of pathologic fungi and the determination and differentiation of these microbes, but more particularly by the severity of the infection and the ever increasing number of persons affected. For a mycologist it is gratifying to realize that greater importance is being attributed to this group of pathogens, but it is just as discouraging to know that not much attention is being paid to the fungi per se.

This work was made possible through a fellowship granted the author by the John Simon Guggenheim Memorial Foundation for study in South America, 1935-1936.

Presented before the Mycological Society of America at the meeting of the American Association for the Advancement of Science at Atlantic City, N. J., Dec. 31, 1936.

Studies, observations and reports from the Laboratory of Mycology, Instituto Oswaldo Cruz, Rio de Janeiro, Brazil (Chief, Dr. Olympio da Fonseca); Department of Microbiology (Section of Mycology), Faculdade de Medicina de São Paulo de Universidade de São Paulo, Brazil (Chief of Section, Prof. Floriano P. de Almeida); Laboratory for Mycology, Bacteriological Institute of the National Department of Hygiene, Buenos Aires, Argentina (Chief, Dr. Pablo Negroni); the Barnard Free Skin and Cancer Hospital, and the School of Medicine, Washington University, Department of Dermatology, service of Dr. M. F. Engman.

In its far reaching distribution blastomycosis is known to include a number of closely allied clinical complications which in their specific locations are found to be due to a definite group of microbes. Accordingly, in the United States, the organism originally isolated by Gilchrist,[1] named by him Blastomyces dermatitidis and now commonly called Zymonema dermatitidis,[2] is usually considered the causative agent of the disease. In Europe the fungus described by Busse,[3] which is now known to be Cryptococcus hominis (Atelosaccharomyces hominis, Torulopsis neoformans), is considered the causative agent. In South America there is a conglomeration of fungi, each of which has been considered as the agent of a blastomycotic type of infection. The confusion in the literature, due to misinterpretations of morphologic phenomena on the one hand and to pseudo-observations on the other, has resulted in numerous publications, some of which are superfluous while others are devoted to clearing up, in a measure, the chaotic problem.

Examining the conditions which at one time or another have been incorrectly diagnosed as blastomycosis, I find that tuberculosis has perhaps been accused of a number of these. Syphilis, with its many clinical manifestations, has been blamed, as has sporotrichosis. These are only two of the many. The main confusion, however, has been found in connection with coccidioidal granuloma, especially in Brazil but also in the United States and other countries of South America. There are a number of yeastlike fungi, particularly in Europe, which in several cases have caused infection that was fatal. In accordance with the opinions of a number of investigators, it is necessary, therefore, to change one's idea as to the organisms of blastomycosis, but only as it applies to the localities in which such situations of conflict or confusion exist.

Several years ago de Almeida[4] compiled a list of the organisms which at one time or another have been considered agents of some type of blastomycosis. This classification I modified somewhat in 1936.[5] To give the reader an idea of the involved situation one is confronted with in this respect, the grouping is here briefly repeated.

---

1. Gilchrist, T. C.: A Case of Blastomycetic Dermatitis in Man, Johns Hopkins Hosp. Rep. **1**:269, 1896.

2. Dodge, C. W.: Medical Mycology, St. Louis, C. V. Mosby Company, 1935, pp. 168-169.

3. Busse, O.: Ueber parasitäre Zelleinschlüsse und ihre Züchtung, Centralbl. f. Bakt. **16**:175, 1894.

4. de Almeida, F. P.: As blastomycoses no Brasil, Ann. Fac. de med. da Univ. de S. Paulo **9**:69, 1933.

5. Moore, M.: La blastomicosis y la cromomicosis de la América del Norte y del Sur, Semana méd. **2**:43, 1936.

The first group in the modified table consists of the organisms causing the saccharomycoses, including such genera as Saccharomyces, Endomyces, Debaryomyces and Hansenula.

The second group includes many yeastlike fungi, some of which are severe pathogens and in several cases have been fatal, producing lesions which are indistinguishable from Gilchrist's blastomycosis. Among these may be considered Torulopsis, Candida, Blastodendrion, Mycotorula or Syringospora, Geotrichum, Mycoderma, Proteomyces and perhaps Neogeotrichum.

These two groups produce lesions not only on the skin but at times in the respiratory and the intestinal tract, and occasionally they produce generalized conditions of the skin or the internal organs.

The typical blastomycosis, however, may be considered to be caused by the organisms of the third group, which consists of the genera Zymonema, Paracoccidioides and Cryptococcus (Atelosaccharomyces). Zymonema is found in the United States with two species, Zymonema dermatitidis and Zymonema capsulatum. Paracoccidioides produces the typical blastomycosis of South America. At present there are two distinct species, Paracoccidioides brasiliensis and Paracoccidioides cerebriformis, each producing definitely distinct clinical lesions. A third species of the same genus, Paracoccidioides tenuis, is described as new in this paper. Cryptococcus (Atelosaccharomyces) in general produces blastomycosis in Europe. There apparently are other yeastlike fungi which may produce a similar histologic picture, which accounts somewhat for the confusion there.

In the fourth group, the family Coccidioideaceae exclusive of Paracoccidioides, there are the genera Coccidioides and Rhinosporidium. Perhaps Histoplasma should be included here, although Ciferri and Redaelli created a new family, Histoplasmaceae,[6] for the genus. The first genus produces coccidioidal granuloma, having as its pathogen, Coccidioides immitis. This condition is prevalent in the United States, and at least three cases have been reported in Argentina. The second genus produces rhinosporidiosis and the third, with the two species Histoplasma capsulatum and Histoplasma pyriforme, causes the distinct disease histoplasmosis.

I shall list a fifth group, not because it belongs among organisms producing blastomycosis, but simply because the name given to it by Terra, Torres, da Fonseca and de Arêa Leão [7] in 1922, has been used

6. Ciferri, R., and Redaelli, P.: Histoplasma Capsulatum Darling, the Agent of "Histoplasmosis": Systematic Position and Characteristics, J. Trop. Med. **37**:278 (Sept. 15) 1934; Caratteri e posizione sistematica dell' agente della "malattia di Darling," Atti dell' Ist. Bot. dell' Univ. di Pavia **6**:247, 1935.

7. Terra, F.; Torres, M.; da Fonseca, O., and de Arêa Leão, A. E.: Novo typo de dermatite verrucosa, mycose por Acrotheca com associação de leishmaniose, Brasil-med. **2**:363, 1922.

rather extensively in such a way as to indicate a relationship with the condition. Further work carried on in Brazil showed that there was no basis for this association. This is the group of organisms producing chromomycosis or—to use the name given the disease by the Brazilian investigators—chromoblastomycosis. A detailed account of this disease and its organisms will be given in another publication.

As this grouping indicates, the subject of blastomycosis, particularly in mycologic and dermatologic literature, is extremely complicated. This is especially so as regards the South American disease, paracoccidioidal granuloma, or as Jordon and Weidman [8] prefer, "de Almeida's disease." This condition is in reality a blastomycosis, due to several fungi of the same genus, which has been confused with Gilchrist's disease and with coccidioidal granuloma. The John Simon Guggenheim Memorial Foundation granted a fellowship to me for study of the South American infections of this category and comparison of them with North American types. This paper, consequently, will be devoted to the study of South American blastomycosis, especially paracoccidioidal granuloma, with a description of the lesions produced and the causative microbes and with references to the comparable or analogous diseases of North and South America and Europe.

The historical aspects of the aforementioned diseases are of interest, and should be summarized briefly, in order to give the reader a general idea of their importance.

COCCIDIOIDAL GRANULOMA

Coccidioidal granuloma was the first disease of this group to be described. The first case was reported by Posadas [9] from Buenos Aires, Argentina, in 1892 as a new case of mycosis fungoides. The same case was reported by Wernicke.[10] in the same year. The second case was described by Rixford [11] and later published with another case by Rixford and Gilchrist.[12] The organism, at first considered a protozoan, was named Coccidioides by Stiles, a medical zoologist. The microbe, however, was found to be a fungus and now bears the name Coccidioides immitis.

---

8. Jordon, J. W., and Weidman, F. D.: Coccidioidal Granuloma, Arch. Dermat. & Syph. **33**:31 (Jan.) 1936.

9. Posadas, A.: Un nuevo caso de micosis fungoidea con psorospermias, An. d. Circ. méd. argent **15**:585, 1892.

10. Wernicke, R.: Über einen Protozoenbefund bei Mycosis fungoides, Centralbl. f. Bakt. **12**:859, 1892.

11. Rixford, E.: A Case of Protozoic Dermatitis, Occidental M. Times **8**:704, 1894.

12. Rixford, E., and Gilchrist, T. C.: Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs: I. First Case Protozoan or Coccidioidal Pseudo Tuberculosis. II. A Second Case of Protozoan Infection, Johns Hopkins Hosp. Rep. **1**:209, 1896.

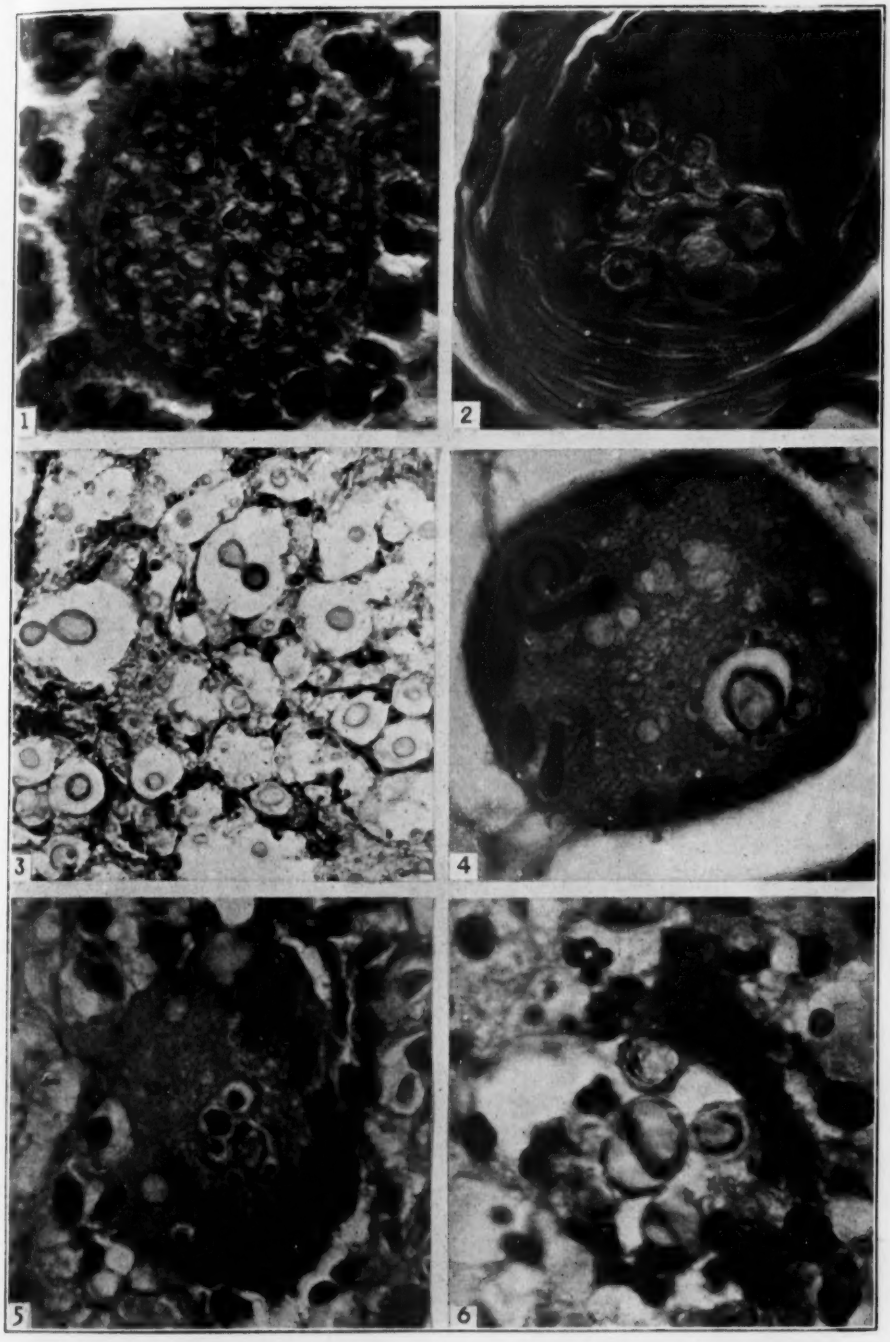


Fig. 1.—(*1*) C. immitis in tissue (oil immersion photomicrograph) removed in a case of Dr. Domingo Mosto, Buenos Aires, Argentina; (*2*) Z. dermatitidis in the plug of a hair follicle (oil immersion photomicrograph); (*3*) C. histolyticus in tissue, showing capsule (oil immersion photomicrograph); (*4*) P. brasiliensis in a giant cell, showing multiple budding (oil immersion photomicrograph); (*5*) P. cerebriformis in a giant cell, showing multiple budding (oil immersion photomicrograph); (*6*) P. cerebriformis, showing multiple budding in tissue (high dry).

The disease may be considered as an infectious granuloma. It may be exceedingly acute and end fatally in a few weeks, or it may be chronic and painful, extending over several years. On the other hand, it may be long drawn out and attended with little pain. Between the first two types there is a third, or subacute, type which is neither rapidly fatal nor unduly prolonged but which is characterized by a definite and positive tendency to widespread dissemination. With this form there are usually associated remissions and relapses, the sufferer living for from six months to two years after infection.

Coccidioidal granuloma is protean in its clinical manifestations and resembles closely a number of other infections. Of chief diagnostic value, however, is the finding of the organism in tissue or in pus, where it presents a typical picture. It reproduces by a process of endosporulation (fig. 1, *1*) forming large mother cells which I am inclined to to call asci, having a diameter up to approximately 80 microns. When these are cultured on artificial mediums, a definite type of mycelium is produced.[13]

Mention must be made here of the fungus Pseudococcidioides Mazzai, so named by da Fonseca.[14] In 1927 Mazza and Parodi obtained slides of material from a prelaryngeal abscess of a patient from the Chaco of Argentina. The sections showed organisms which appeared to these two investigators as similar to C. immitis. Da Fonseca, however, studied the slides and named the organism P. Mazzai. The fungus was never cultured. De Almeida,[15] working with a strain of C. immitis from the United States, found similar pictures in material taken from his experimental animals. There is no doubt that the organism of Mazza and Parodi was only a variant of C. immitis, as shown by de Almeida.[16]

According to the work of da Fonseca and de Arêa Leão,[17] coccidioidal granuloma due to a different species of fungus is present in Brazil. A study of over 150 cultures isolated in cases of supposed infections of this nature in Brazil gave only the various species of Paracoccidioides that are being described in this paper. The difference

13. Moore, M.: Coccidioidal Granuloma: A Classification of the Causative Agent, Coccidioides Immitis, Ann. Missouri Botan. Garden **19**:397, 1932.

14. da Fonseca, O. O. R.: Ensayo de revisión de las blastomicosis sudamericanas, Bol. Inst. de clín. quir. **4**:469, 1928.

15. de Almeida, F. P.: Considerações em torno do Coccidioides immitis e do Pseudococcidioides mazzai, Ann. Fac. de med. da Univ. de S. Paulo **7**:83, 1932.

16. de Almeida, F. P.: Nota a proposito de Coccidioides immitis e Pseudococcidioides mazzai, Ann. Fac. de med. da Univ. de S. Paulo **10**:29, 1934.

17. da Fonseca, O. O. R., and de Arêa Leão, A. E.: Sobre o granuloma coccidioidal. Formas de evolução nos tecidos, no pus dos ganglios lymphaticos e nos culturas do "Coccidioides immitis," Posição systematica do parasito, Bol. Inst brasil. sc. **3**:21, 1927.

in the diseases was brought out clearly by de Almeida in his series of papers and by me in several South American publications.[18] Recently, Jordon and Weidman [8] corroborated de Almeida's work, using two South American strains. As far as I could determine from the literature, only two cases of coccidioidal granuloma have been published in South America. In a third case Professor Domingo Mosto of the Rawson Hospital, Buenos Aires, Argentina, made a diagnosis of osseous blastomycosis with generalization (fig. 1, *1* is of material studied in this case). Additional cases from Argentina are being reported.

BLASTOMYCOSIS

The next disease entity, blastomycosis, covers one of the greatest groups of infections classified under one term. Its universal presence has given it added importance. As mentioned previously, blastomycosis may be divided into three groups: North American, European and South American. The first actual case of North American blastomycosis, so-called, was reported by Gilchrist at the June 1894 session of the American Dermatological Association. His paper was presented as the result of finding of peculiar yeastlike bodies in the diseased tissue of a patient. The condition was diagnosed by the attending physician as typical, chronic scrofuloderma. Approximately two years later this case was reported in detail by Gilchrist.[1] In 1896 Curtis [19] isolated a fungus supposedly similar to that described by Gilchrist from a myxomatous tumor of the leg. In the same year Gilchrist, in conjunction with Stokes,[20] published a short paper on a second case of blastomycosis, and a detailed report of this was published two years later.[21]

Clinicians have usually referred to the category of blastomycosis any clinicopathologic condition which might be due to yeastlike or budding fungi. This point of view, however, is being rapidly changed, owing to a better understanding of mycoses in general. Blastomycosis presents numerous clinical manifestations, and in this respect it is protean, being found in practically every organ of the human body, either

18. Moore, M.: (*a*) A New Species of the Genus Paracoccidioides Almeida (1930): P. Cerebriformis Moore, (1935), Rev. biol. hyg. **6**:148, 1935. (*b*) Un nuevo tipo clínico de blastomicosis producido por Paracoccidioides cerebriformis n.s., Arch. urug. de med., cir. y especialid. **8**:224, 1936. (*c*) La blastomicosis en las Américas del Norte y del Sud, Rev. argent. derm. sif. **20**:448, 1936.

19. Curtis, F.: Contribution a l'étude de la saccharomycose humaine, Ann. Inst. Pasteur **10**:449, 1896.

20. Gilchrist, T. C., and Stokes, W. R.: The Presence of an Oidium in the Tissues of a Case of Pseudo-Lupus Vulgaris, Bull. Johns Hopkins Hosp. **7**: 129, 1896.

21. Gilchrist, T. C., and Stokes, W. R.: A Case of Pseudo-Lupus Vulgaris Caused by a Blastomyces, J. Exper. Med. **3**:53, 1898.

in biopsy or in autopsy material. Clinically, lesions may be found which are alike both for the cutaneous (fig. 2) type of the disease—that is, that group of infections which may be found occurring superficially—or for the systemic type, occurring in the lungs, the bones, the meninges, the liver or other viscera. The lesions may be granulomatous. The division into a cutaneous and a systemic type, based on the work of Jacobson,[22] may be extended, the cutaneous form being primary when it occurs in the epidermal layers or the cutis or secondary when it is due to an infection of the deeper tissues, the internal viscera or the bony structures. Each subdivision presents several different pictures, which have been discussed by Jacobson [22] and by me.[23]

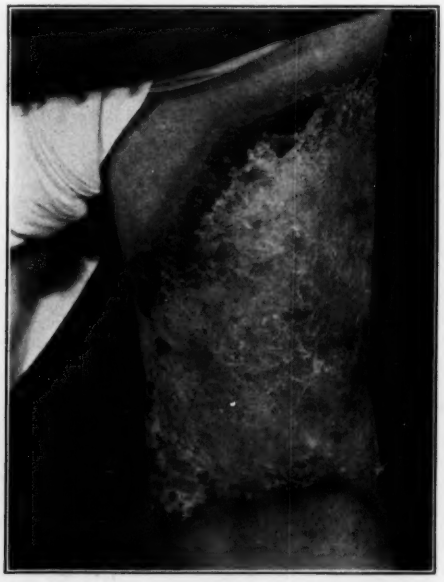


Fig. 2.—Lesion of cutaneous blastomycosis (Gilchrist's disease).

In Gilchrist's disease the organism seen in tissue or in pus consists usually of spherical, simple or budding yeastlike cells, which may vary from 5 to 12 microns in diameter (fig. 1, *2*). In old lesions one may see occasionally simple branching cells, which sometimes are as long as 20 microns. When grown on artificial mediums, the fungus acquires a filamentous mycelium characterized by a number of specialized structures and cells which typify the organism, namely, Zymonema dermatitidis [23] (Blastomyces, Endomyces).

22. Jacobson, H. P.: Fungous Diseases: A Clinico-Mycological Text, Springfield, Ill., Charles C. Thomas, Publisher, 1932, pp. 149-181.

23. Moore, M.: Blastomycosis: Report of a Case, with a Study of an Etiologic Factor and a Classification of the Organism, Ann. Missouri Botan. Garden **20**:79, 1933.

European blastomycosis dates back to several months after Gilchrist's publication, when Busse brought to light the extraordinary condition to which he later gave the name saccharomycosis hominis.[24] The patient was a 31 year old woman who had suffered from a localized, subperiosteal inflammation of the left tibia. An examination of the abscess, which opened spontaneously, revealed "numerous, doubly-contoured, very refractive, roundish and ovoid bodies," which were found intracellularly and extracellularly in the pus and in the wall of the abscess. Superficial ulcers later developed on the face, and subperiosteal swellings appeared on the right ulna and the left sixth rib, near the axillary line. Death ensued. Busse cultured the yeast from the ulnar swellings and from the bottom of the ulcers.

Clinically, this blastomycosis may be subdivided in a fashion similar to that used in classifying Gilchrist's disease, namely, into cutaneous and systemic types. Here, however, one usually finds the ulcerative type of lesion in the cutaneous form, which histopathologically shows abscesses with few leukocytes and little inflammation. Within these abscesses are found spherical to ovoid simple or budding yeastlike cells which measure from 5 to 10 microns in diameter, usually about 8 microns. When seen in tissue or in pus, the cells of this fungus are surrounded by a thick, mucoid, refractile capsule which does not stain ordinarily or, if at all, lightly (fig. 1, *3*). When cultured, the organism consists only of budding cells, with no mycelium or pseudomycelium, a characteristic of the genus Cryptococcus.

South American blastomycosis, or paracoccidioidal granuloma, comprises the third group of blastomycoses, exclusive of coccidioidal granuloma, which will be discussed here. The disease was first described by Lutz [25] in 1908, when he considered it a pseudococcidioidal granuloma, with the organisms occurring chiefly in giant cells. The fungus, which seemed to have the appearance of Oidium lactis, was isolated in pure culture from the lymphatic and the salivary glands of the patient. In the same year Carini [26] described a case in which there were primary lesions in the buccal mucosa. In 1909 Splendore described a case of generalized blastomycosis. Thus, attention was called to two clinical types, the localized form, with the lesions in the buccal mucosa and the organism generally found in giant cells (pseudococcidioides), and the generalized form. Splendore expressed the belief that these two forms were due to two different micro-organisms. Then followed several

24. Busse, O.: Ueber Saccharomycosis hominis, Virchows Arch. f. path. Anat. **140**:23, 1895.

25. Lutz, A.: Uma mycose pseudococcidica localisada na bocca e observada no Brasil. Contribuição ao conhecimento das hyphoblastomycoses Americanas, Brasil-med. **22**:121 and 141, 1908.

26. Carini, A.: Un caso de blastomycose con localisação primitiva na mucosa da bocca, Rev. da Soc. de sc. S. Paulo **3**:120, 1908.

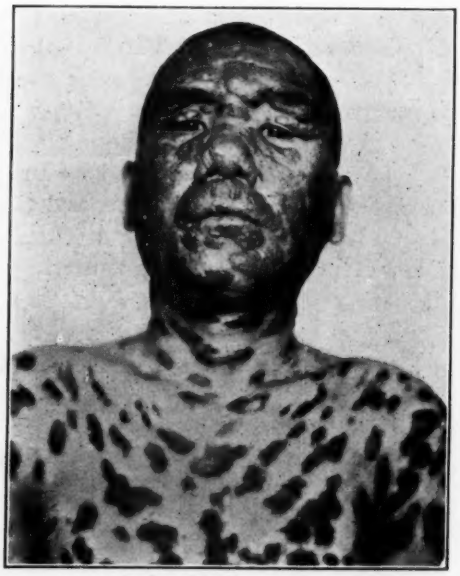


Fig. 3.—Lesion of paracoccidioidal granuloma (generalized type).

Fig. 4.—Lesion of paracoccidioidal granuloma (localized type affecting the buccal mucosa).

reports by this same worker, and in 1912 [27] he established the specific name of brasiliense for the organism, supplied a short description and placed it in the genus Zymonema of De Beurmann and Gougerot.[28] This

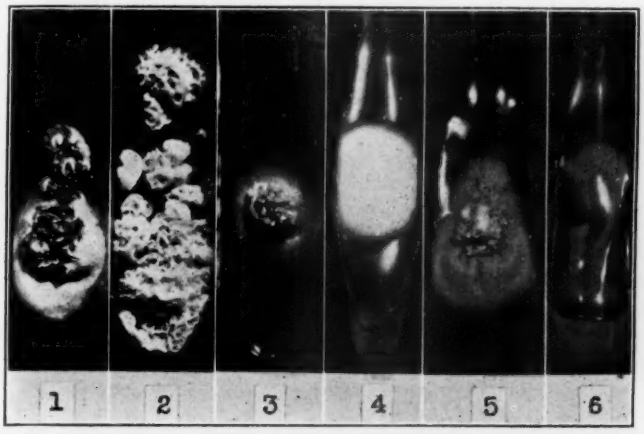


Fig. 5.—Cultures of organisms on glycerin agar: (*1*) P. brasiliensis; (*2*) P. cerebriformis; (*3*) P. tenuis; (*4*) C. immitis; (*5*) Z. dermatitidis; (*6*) C. histolyticus.

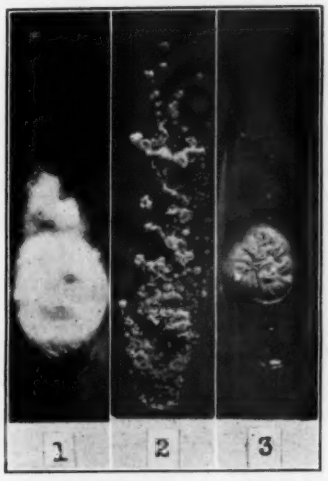


Fig. 6.—Cultures of species of Paracoccidioides on malt extract agar: (*1*) P. brasiliensis; (*2*) P. cerebriformis; (*3*) P. tenuis.

27. Splendore, A.: Zymonematosi con localizzazione nella cavitè della bocca, osservata in Brasile, Bull. Soc. path. exot. **5**:313, 1912.

28. De Beurmann, L., and Gougerot, H.: Les Exascoses, Endomycoses et Parendomycoses (muguet). Saccharomycoses (mycose de Busse-Buschke) et Parasaccharomycoses. Zymonematoses (mycose de Gilchrist), Bull. et mém. Soc. méd. d. hôp. de Paris **28**:222, 1909.

report was followed by a more lengthy description the following year.[29] There followed then a number of reports of cases.

Clinically, paracoccidioidal granuloma may be divided into two main groups,[18c] the generalized form (fig. 3) due to P. brasiliensis or to P. tenuis and the localized type affecting the buccal mucosa (fig. 4), due to P. cerebriformis. The generalized disease may be acute or chronic. The fungus may enter the buccal cavity by way of the mouth, lodging

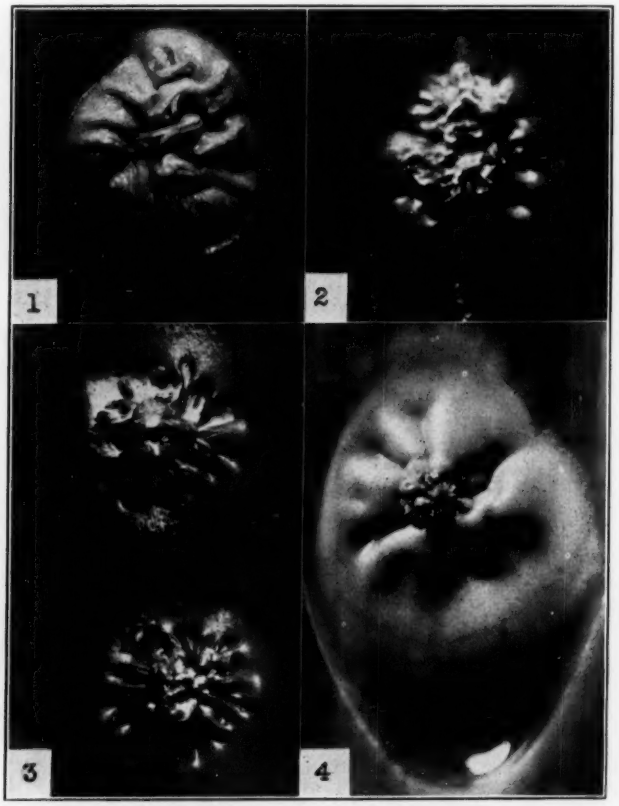


Fig. 7.—Cultures of P. tenuis on (*1*) malt extract agar; (*2*) peptone agar; (*3*) Sabouraud's maltose agar; (*4*) glycerin agar.

usually in the gums and forming a hard infiltration which spreads to the lips, the nose and the margin of the tongue. This presents a histologic picture of granuloma. A pseudotuberculous papule may be produced on the uvula, and a papillomatous vegetation may develop on the tonsils and the gingiva, giving the appearance of an acuminate

29. Splendore, A.: Un' affezione micotica con localizzazione nella mucosa della bocca, osservata in Brasile, determinata da funghi appartenenti alla tribù degli Exoascei (Zymonema brasiliense, n. sp.), in Onore del Prof. Angelo Celli nel 25 anno di insegnamento, Turin, 1913, p. 421.

condyloma. The ulcerative processes may spread to the skin, presenting likewise vegetative and papillomatous lesions on the body. In generalized infections of the skin the primary lesion may have developed as the result of an abrasion or wound where the fungus has become lodged, with subsequent pathologic change.

In many cases of chronic blastomycosis the lesions are localized in the mouth (fig. 4). However, the invading germ may penetrate into the tonsils and thus cause the disease to become generalized within the body by means of the lymphatic system. In cases in which the condition is due to P. cerebriformis this happens only in the terminal stage of the disease. In cases in which it is due to P. brasiliensis or to P. tenuis the organism may attack a priori the tonsils, producing acute ulceration and inflammation, with a localized lymphangitis which soon becomes generalized. There is developed, then, a typical granulomatous condition of acute blastomycosis.

The infection of the skin at times may simulate Gilchrist's disease or coccidioidal granuloma. However, in addition to the features aforementioned, it may be nodular, somewhat verrucoid and vegetative.

When seen in tissue or in pus, the fungi are of two different types, which often require careful examination. In the first place, the organisms all show the simple and budding cells characteristic of Z. dermatitidis. This is one reason why cases reported from South America have been considered instances of Gilchrist's disease.[30] When slides of tissue that show this feature are examined, it is extremely difficult to differentiate the two diseases histologically. There are, in addition, certain properties which are attributable to the South American fungi which are not found in Z. dermatitidis, such as multiple budding. This process is the same for the three species of Paracoccidioides, but there are slight differences in the sizes of the cells and the gemmules. P. brasiliensis and P. tenuis when seen in tissue or in pus are spherical or ovoid, from 1 to 30 microns in diameter (rarely larger) and double contoured, with simple or multiple budding of minute, spherical, ovoid or bacillary gemmules of a diameter of approximately 1 micron or more. The multiple budding is particularly seen in giant cell formation (fig. 1, *4*). P. cerebriformis, on the other hand, when seen in tissue or in pus is spherical or ovoid, from approximately 3 to 30 microns in diameter (rarely larger, but uniformly larger than the two other species) and double contoured, with single or multiple budding of small spherical,

30. Talice, R. V., and MacKinnon, J. E.: Primer caso de blastomicosis (tipo Gilchrist) observado en el Uruguay, Arch. urug. de med., cir. y especialid. **3**: 177, 1933. Niño, F. L.: Ulceración blastomicética cutáneomucosa del labio inferior, Soc. argent. de pat. reg. **5**:213, 1929. Mazza, S.; Niño, F. L., and Nicolini, R.: Blastomicosis de la mucosa labiogeniana, ibid. **5**:231, 1929. Niño, F. L., and Perez, B.: Blastomicosis de la mucosa gingivo-geniana, ibid. **7**:413, 1931.

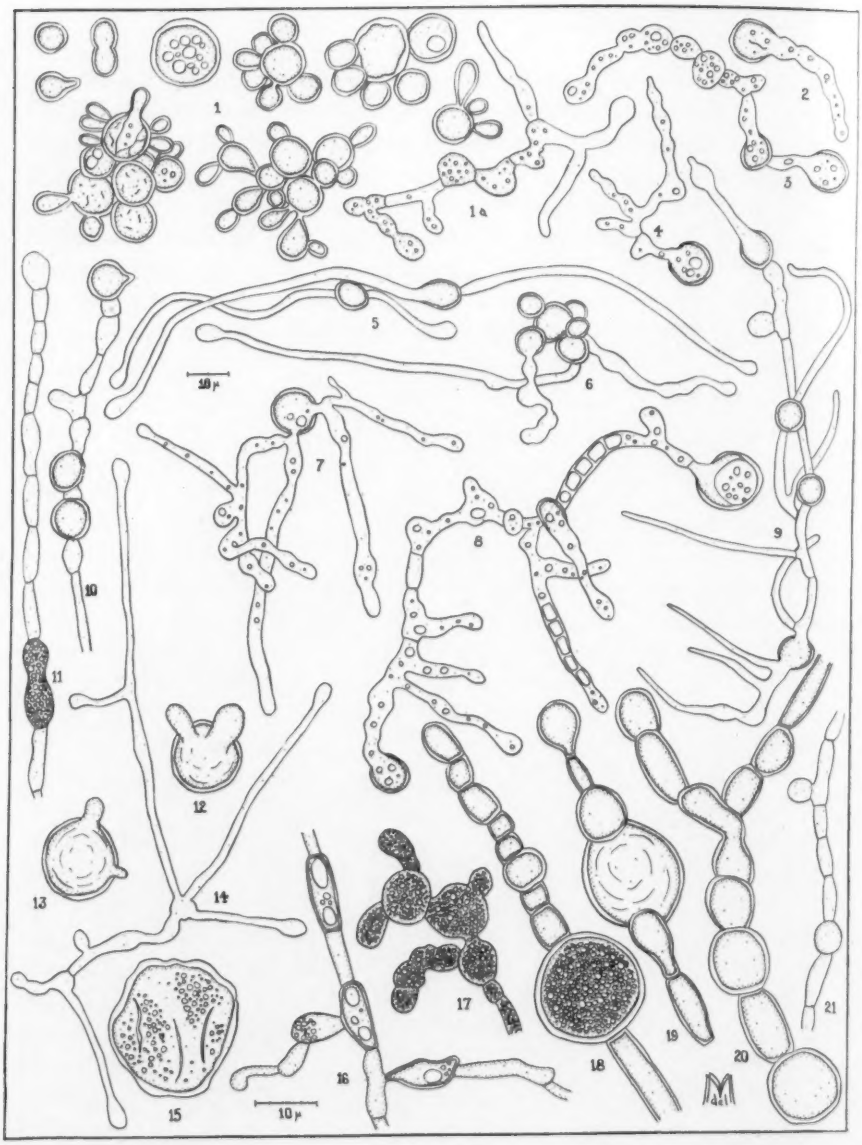


Fig. 8.—P. brasiliensis. All the drawings were made with the aid of a camera lucida and reduced: parts *1-11, 14* and *21* are reproduced at a magnification of × 1,060 and nos. *12, 13* and *15-20* at a magnification of × 1,960. Part *1* shows various forms of cells seen in pus, some with multiple budding; *1a*, a filament seen in pus incubated twelve days; *2, 3* and *7*, filaments of twelve days' growth on Sabouraud's maltose agar; *4* and *8*, filaments of twelve days' growth on peptone agar; *5* and *6*, filaments of ten days' growth on Sabouraud's dextrose agar; *9*, an eighteen day growth on Sabouraud's dextrose agar; *10, 11* and *21*, mycelial structures thirty-two days old on Sabouraud's dextrose agar; *12* and *19*, large cells and hyphal cells on malt extract agar; *13*, growth on glycerin agar; *14*, a fourteen day growth on Sabouraud's maltose agar; *15* and *17*, growths on peptone agar with large, spherical cells and typical mycelial structures; *16*, a type of growth on Sabouraud's dextrose agar, and *18* and *20*, cells on peptone agar.

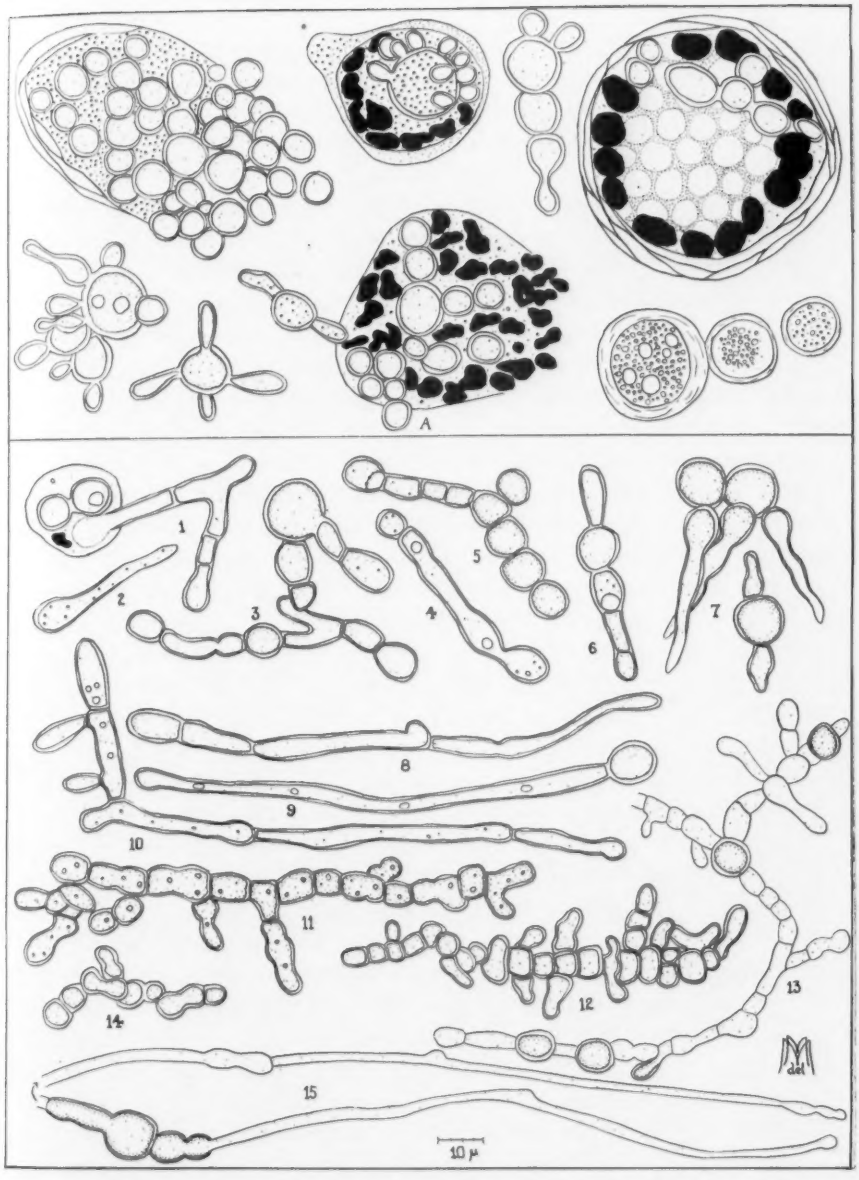


Fig. 9.—P. cerebriformis. All the drawings were made with the aid of a camera lucida at a magnification of × 1,050 and reduced. *A*, presents types of cells seen in pus, showing multiple budding cells of different forms and phagocytosed organisms in giant macrophages; *1-6*, germinating cells after three days on Sabouraud's maltose agar; *7*, germinating cells after five days on peptone agar; *8-10*, young filaments after seven days on Sabouraud's maltose agar; *11, 12* and *14*, hyphae after twelve days on Sabouraud's maltose agar; *13*, a hypha after thirty-eight days on Sabouraud's maltose agar, and *15*, a long filament formed after eight days on peptone agar.

ovoid or elongated gemmules, of a diameter of approximately 3 microns or more. These may be seen in giant cells (fig. 1, *5*) and distributed freely in the pus or the tissue (fig. 1, *6*). In addition, P. cerebriformis may be found in giant macrophages of the pus, simulating the picture of C. immitis (fig. 9, A). Organisms of this type have been called pseudococcidioides and have confused South American workers. These huge macrophages are not usually seen in pus infected with P. brasiliensis or P. tenuis. The organisms here, however, show multiple budding, growing freely in the midst of the pyogenic cells (fig. 8, *1*).

The interpretation of these buds has led to a little nomenclatorial confusion. In the first place, the arrangement or disposition of these gemmules caused Haberfeld [31] to change the species name to histosporocellularis. On the basis of the latter's work, Arantes [32] and then da Fonseca and de Arêa Leão considered the organisms as of the genus Coccidioides, interpreting these gemmules as preformed sporules which emerge simultaneously from the mother cell or supposed ascus through stomata, or slits that are formed in the wall of the ascus. Accordingly, on emerging, a spore wall is produced around the material.

When seen in stained (hematoxylin and eosin) sections of tissue, the fungi show a number of irregular granules. These may appear to be spread throughout the entire cell but usually seem to be disposed along the inner surface of the wall of the cell. Fine filaments may be seen connecting these granules and shedding light on their nature, that of metachromatic granules. Unless they are examined critically, their appearance gives the mistaken impression that they are spores. It is these granules which form the coronet so often described by other authors. Their number and amount are subject generally to the age of the cell. Young cells which have just budded off from the mother cell have little metachromatic material. Older or more mature cells have much more of this substance, while organisms which are ready for gemmation have a great number, all of which appear rather uniform. This adds further confusion, as they tend to round up and form what might be interpreted as nuclei. In the process of multiple budding the granules enter the buds while these are developing, much as do nuclei. During this process the picture presented would appear to indicate that a channel is formed through the wall of the mother cell which serves as an outlet for the material within the cell. It was a misinterpretation of this phenomenon that influenced the writings of Haberfeld, Arantes, da Fonseca and de Arêa Leão. What actually happens is that the metachromatic material seen in the histologic sections takes the stain and is

31. Haberfeld, W.: Granuloma ganglionar maligno, de origem "Blastomycetica" (Zymonema histosporocellularis), Secção de Obras d'O Estado de São Paulo, São Paulo, 1919.

32. Arantes, A.: Lymphogranuloma maligno de origen Coccidioide, Thesis, Faculdade de medicina cirurgia de São Paulo, 1922.

therefore visible to the eye, while the membrane of the developing gemmule, being thin and young, takes the counterstain lightly if at all and consequently is not seen by the observer. It is difficult to conceive of metachromatic material—for such the material is—emerging naked from a cell and then acquiring a capsule when it is outside the mother structure. An analogy may be drawn with the animal fetus. It is highly improbable that at birth the internal organs would emerge first, giving rise subsequently to a protective covering of tissue, namely, the epidermis.

It can readily be seen, therefore, that the suggestion that these structures are spores in the tissue is entirely erroneous. They do not dehisce through apertures in the membrane of the mother cell, as has been explained previously.

The foregoing descriptions of lesions and of the organisms, if put on a comparative basis, present a number of distinct features, as shown in table 1. The chief importance of this comparison lies in the structure of the fungi seen in the tissue or the pus in cases of the different diseases.

MATERIALS AND METHODS

The cultures and material studied were obtained from various sources in different countries. The clinical information and the fungi relative to the North American disease were obtained from the Barnard Free Skin and Cancer Hospital and the Barnes Hospital, service of Dr. Martin F. Engman, St. Louis. The cultures and clinical data on the South American disease were obtained from Drs. Olympio da Fonseca, Magarinos Torres and Souza Arouja of the Instituto Oswaldo Cruz and the Hospital for Dermatology and Syphilology, service of Dr. Eduardo Rabelo, Rio de Janeiro, Brazil; Dr. Floriano P. de Almeida, Professor of Microbiology, Faculdade de Medicina de São Paulo de Universidade de São Paulo, Brazil, and Santa Casa de Misericordia de São Paulo, Dermatological Clinic, service of Dr. A. Lindenberg, São Paulo, Brazil; Dr. Pedro L. Baliña, Professor of Dermatology, University of Buenos Aires, Argentina; Dr. Pablo Negroni, Bacteriological Institute of the National Department of Hygiene, Buenos Aires, Argentina, and Dr. Flavio Niño, Laboratory of the Institute of Clinical Surgery, Hospital de Clinicas (director, Professor José Arce), Buenos Aires, Argentina.

The pus and the tissue were examined for fungi and the histologic features. Sections of tissue were stained with hematoxylin and eosin. Cultures inoculated with pus from the patient were studied, and the subsequently developing cultures were subcultured on various mediums, in order to determine the effects of varied substrates on the growth. Hanging drop preparations, as well as agar slides inoculated with infected material, were used for observation of the developing microbes.

The biochemical reactions, including fermentation of carbohydrates, liquefaction of gelatin and acidification and curdling of litmus milk, were carried out under similar conditions for all the organisms, similar material being used for each fungus.

Microscopic preparations of the different cultures of the various fungi were made in methylene blue and glycerin (1 per cent aqueous solution of methylene blue in glycerin to the desired intensity) to study the morphologic phenomena on the different substrates. Drawings were made with the aid of a camera lucida.

TABLE 1.—*Clinical and Mycologic Differentiation of Coccidioidal Granuloma, Blastomycosis and Paracoccidioidal Granuloma (North American, South American and European)*

Disease	Fungus	Clinical Characteristics	Organisms in Tissue or in Pus	Gross Cultures	Microscopic Cultural Appearance
Coccidioidal granuloma (Posadas' disease, 1892) (Rixford and Gilchrist, 1894) (Rixford and Gilchrist, 1894)	Coccidioides immitis	Infectious granuloma; acute, subacute or chronic; protean, with lesions either cutaneous, subcutaneous or systemic, involving generally the respiratory system; lesions may be nodular, ulcerative, papillomatous, verrucoid, resembling a gummatous tumor or a cold abscess	Cells isolated or in giant cells; spherical, thick walled with a reported diameter of approximately 2-80μ; reproduces by endospore formation (ascus); budding absent; wall of ascus often showing radiate formation	Colonies flat, somewhat submerged, grayish, becoming white to light cream, with aerial hyphae; cottony, at times coremioid; color changes to light chamois and to smoky brown with age; growth rapid	Hyphae septate, branching, 0.5-4μ in diameter; hyphal swellings, arthrosporous cells 2.5-7μ in diameter, 5-12μ in long axis; chlamydospores abundant, 5-8μ in diameter; racquet mycelium; terminal hypnospores approximately 5 $\times$ 8μ; endogenous spore formation in anaerobic conditions
North American blastomycosis (Gilchrist's disease, 1894)	Zymonema dermatitidis Zymonema capsulatum Zymonema capsulatum var. Isabellinus	Infectious condition often granulomatous; acute to chronic; protean, with lesions cutaneous or systemic; cutaneous lesions primary or secondary, papulo-ulcerative, verrucous or papillomatous, gummatous, showing typical violaceous color	Simple or budding yeastlike cells, thick walled, approximately 5-20μ in diameter, usually approximately 7μ	Colonies in general at first yeastlike, then prickly (coremioid), finally profuse and cottony, changing from white to chamois then to cinnamon and to brown; show radiating ridges and concentric rings of growth; Z. capsulatum remains white, and var. Isabellinus is a light chamois; growth rapid	Hyphae septate, branching, 2-4μ in diameter; conidia pyriform or round, pedicellate or sessile, 5μ in diameter; racquet mycelium; 5-6 $\times$ 3.5μ; chlamydospores terminal or lateral, 5.5-7.5 $\times$ 12-15μ or spherical, 7μ in diameter; ascogenous cells spherical, 8-13μ in diameter
European blastomycosis (Busse-Buschke's disease, 1894)	Cryptococcus hominis Atelosaccharomyces hominis (Torulopsis neoformans)	Similar clinically to Gilchrist's disease but ulcerative type common in cutaneous form, with abscesses, little inflammation; usually found invading cerebrospinal system	Thick-walled, heavily encapsulated, simple or budding cells approximately 5-10μ in diameter, occasionally larger, usually approximately 8μ	Colonies yeasty or pasty, smooth, mucoid to moist, subpulvinate; color light cream, becoming light tan to brown with age; growth fair	Spherical to ovoid budding, encapsulated cells approximately 2-6μ in diameter, rarely larger; no mycelium, pseudomycelium or spores
South American blastomycosis Paracoccidioidal granuloma (Lutz-Splendore-de Almeida disease, 1908) A. Generalized type B. Localized type affecting the buccal mucosa	(*a*) Paracoccidioides brasiliensis (*b*) Paracoccidioides tenuis (*c*) Paracoccidioides cerebriformis	A. Generalized or localized, cutaneous or systemic, granulomatous, papulous, verrucous or ulcerative; acute to chronic; usually lymphangitic in spread B. Lesions localized on buccal mucosa; acute to chronic; verrucous, papillomatous; ulcerative, granulomatous; lymphangitic spread only in terminal stage	(*a*) and (*b*) Cells spherical or ovoid 1-30μ in diameter, rarely larger, with thick walls; simple or multiple budding of minute, spherical, ovoid or bacillary gemmules, of approximately 1μ and larger (*c*) Cells spherical or ovoid, 3-30μ in diameter, rarely larger, but uniformly larger than those of P. brasiliensis or P. tenuis; thick walled, with simple or multiple budding of small, spherical, ovoid, or elongated gemmules of approximately 3μ or over; cells often found in giant macrophages (pseudococcidioides)	(*a*) White, adherent to substratum and somewhat hard, well defined, somewhat cottony; colonies become light tan with age; growth slow (*b*) Mycelium mostly submerged; colonies compact, verrucoid or vermiculate at inoculation, showing folds or radiating ridges; white, becoming light tan with age; growth slow (*c*) On agar, cerebriform to vermiculate, yeastlike, creamy buff, becoming light cinnamon-buff with age; easily separated from substratum, but filamentous, flat and adherent to dry portions of substratum; growth slow	(*a*) Hyphae septate, branching, 1.5-3.5μ; hyphal swellings 3-5μ; spherical, terminal chlamydospores up to 15μ; intercalary chlamydospores 6-10μ; irregular sclerotic, intercalary cells 7 $\times$ 15μ; conidia lateral, sessile or pedicellate, 3-7μ (*b*) Same as P. brasiliensis, except that corresponding structures are smaller (*c*) Hyphae irregular, septate, branching, 2-7μ in diameter, with many swellings; cells arthrosporous, oidioid, dumbbell shaped; chlamydospores spherical, elongate, pyriform or sclerotic, intercalary, lateral or terminal, up to 15μ; conidia lateral, spherical or pyriform, 3-10μ

DESCRIPTIONS OF ORGANISMS

Since the fungi of coccidioidal granuloma and Gilchrist's North American blastomycosis have been considered in detail in other publications,[33] such consideration will not be given them here. The yeast-like development of the microbes producing European blastomycosis is of the simple budding type of Cryptococcus, as has been mentioned previously. This paper, therefore, will be devoted chiefly to the fungi of South American blastomycosis or paracoccidioidal granuloma, or—if the phrase is preferred—Lutz-Splendore-de Almeida disease.

Paracoccidioides brasiliensis (Splendore) de Almeida, Ann. Fac. de med. da Univ. de S. Paulo **5**:1-19, 1930.

Zymonema brasiliense Splendore, Bull. Soc. path. exot. **5**:313-319, 1912.

Zymonema histosporocellularis Haberfeld, Granuloma ganglionar maligno de origem "Blastomycetica" (Zymonema histosporocellularis), São Paulo, 1919.

Coccidioides histosporocellularis Arantes, Lympho-granuloma maligna de origem "Coccidioide," Thesis, São Paulo, 1922.

Coccidioides brasiliensis de Almeida, Ann. Fac. de med. da Univ. de S. Paulo **4**:91-98, 1929.

Monilia brasiliensis Vuillemin, Les champignons parasites et les mycoses de l'homme, Paris, Paul Lechevalier, 1931, p. 86.

Coccidioides histo-porocellulare da Fonseca, cited by Zeisler, E. P.: Arch. Dermat. & Syph. **25**:68, 1932.

Coccidioides esferiformis Moore, Ann. Missouri Botan. Garden **19**:397-428, 1932.

When seen in tissue or in pus, the organism consists of simple single or multiple budding cells, spherical or ovoid, double contoured and from 1 to approximately 30μ in diameter (fig. 8, *1*). The gemmules are small, spherical and avoid or bacillary, the latter form being seen mostly in tissue while the former prevails in pus. The multiple budding process begins by the concentration of the dispersed metachromatic material in the mother cell in the form of a coronet along the inner surface of the cell membrane. When the cell becomes mature, the wall pushes out, taking with it some of this material. There is a typical pinching in of this outgrowth, characteristic of budding, and the young bud goes on to development, separating itself from the mother structure. In the moist pus this procedure is more apparent, since the cells are generally larger. In the tissue or in giant cells the gemmules are smaller and consequently more difficult to see. In addition, as mentioned previously, the wall of the young germinating cell does not take the eosin easily, so that the observer may often misinterpret it as a spore emerging from the maternal cell. Mycelial structures are never seen in tissue but may be noticed rarely in pus and then only in old or necrotic lesions (fig. 8, *1a*).

When agar is inoculated with pus containing these cells, a culture develops which consists of a branching, septate mycelium, filamentous, cottony or yeast-like, with intercalary, lateral or terminal chlamydospores, conidia, sclerotic cells and hyphal swellings of various proportions.

It was observed in hanging drop and other preparations that the cells after approximately the fourth day start to germinate, sending out small tubes. These

33. Moore.[13] Moore.[23]

develop slowly until about the tenth day, when there is definite, macroscopically apparent growth (fig. 8, *5* and *6*). At this time the tubes have become elongated, extending out in one or several directions from the mother cell. These may have terminal enlargements, as on Sabouraud's dextrose or maltose agar, or somewhat blunt ends. Cells with multiple buds germinate in much the same manner, giving the picture seen in *6* of figure 8. As the culture becomes older, after the twelfth day, the filaments become more complicated, acquiring branches, intercalary enlargements or oidioid cells, cross walls and conidium-like cells (fig. 8, *2* to *8*). The type of substratum on which the organism is growing is responsible for the size and the structure of the mycelial constituents. Consequently, the filaments and the cells may be somewhat large, as in *8* of figure 8; they may be narrow, long and fine (fig. 8, *14*), or they may consist of short, fine cells. The progressive mycelial changes become more marked on the eighteenth day, including then intercalary and terminal, thick-walled cells, probably chlamydospores (fig. 9, *9*), which become more apparent in older cultures (fig. 8, *10*, *11* and *21*).

In addition to the aforementioned features, the filaments acquire cross walls in the hyphae to produce arthrospore-like cells (fig. 8, *11*, *16*, *18* and *21*). As the cells become older, these structures become thick walled, enlarged and somewhat rounded or slightly elongated (fig. 8, *20*) and are finally set free to produce, with the liberated chlamydospores, the huge number of round forms seen in older cultures. The spherical cells become more enlarged and show large numbers of droplets of oil or materials for storage (fig. 8, *15*, *17* and *18*) and may be interpreted as resting cells or chlamydospores. Under favorable conditions they may germinate and appear in much the same manner as do the cells in tissue or in pus (fig. 8, *12* and *13*).

Macroscopically the organism assumes somewhat different characteristics on different mediums. When grown on Sabouraud's maltose agar, it is at first the color of the substratum; then, as the aerial hyphae develop, it becomes white and in some instances changes to a light chamois. On malt extract agar and wort agar the colonies are cottony, somewhat heaped up in the center and dull creamy white. Old cultures tend to become heaped up in the center, cracked or fissured, particularly on glycerin agar. The aerial hyphae are short and not especially cottony and in the dryer portion of the slant take on a powdery appearance. The color changes to a light tan, while some strains remain white, with a somewhat bluish tinge. The colonies are compact, somewhat hard and adherent to the substratum.

The mature growth, therefore, shows septate and branching hyphae which measure approximately 1.5-3.5μ in diameter, with hyphal enlargements 3-5μ in diameter. The chlamydospores are spherical, terminal or intercalary and of approximately 6-15μ. The terminal cells are usually much larger, with some attaining a diameter, after liberation, of approximately 30μ. Irregular, sclerotic, intercalary cells measure $7 \times 15\mu$, while the lateral, sessile or pedicellate conidia are 3-7μ in axis.

Paracoccidioides cerebriformis Moore, Rev. biol. e hyg. **6**:148-154 (Dec.) 1935.

(Synonomy similar to that of P. brasiliensis.) When seen in tissue or in pus, the cells present much the same appearance as that characteristic of P. brasiliensis, except that the budding cells or gemmules are uniformly larger than the former, measuring approximately 3μ or more. Here, too, one may see single or simple budding organisms similar to those found in Gilchrist's disease, measuring up to approximately 30μ and averaging about 15μ. The multiple budding of P. brasiliensis is evident in P. cerebriformis, distributed freely in the pus, the tissue and the giant cells. In addition to these features, there may be seen in pus huge giant

cells or macrophages, within which may be found the phagocytosed fungi in the various forms mentioned (fig. 9, *A*). This feature appeared only in cases in which the condition was produced by P. cerebriformis and seems to be a characteristic of that organism. A number of these phagocytic macrophages containing fungi simulate C. immitis so closely that unless the budding forms were seen one might be inclined to diagnose the disease incorrectly.

Artificial growth is macroscopically evident between the sixth and the tenth day as dull, flat, creamy yellow colonies which are slightly adherent to the substratum. Germination of the cells is microscopically evident on the third day, particularly on peptone agar (fig. 9, *1* to *6*). The germinating cells show somewhat different morphologic phenomena from those which characterize P. brasiliensis. The developing filaments are shorter and larger in diameter, with an early formation of septums, so that the cells appear as arthrospores (fig. 9, *5*). On mediums containing some carbohydrate the filaments tend to be more elongate and smaller in diameter (fig. 9, *8* to *10*). Occasionally, however, fine filaments may be seen on peptone agar (fig. 9, *15*), these being extremely few. As the organism becomes older, on the twelfth day, its wall is somewhat thickened, and the filaments form arthrospore-like cells (fig. 9, *11, 12* and *14*). These persist for some time, but eventually, as on Sabouraud's maltose agar after thirty-eight days become thin and more spread out. This varies, of course, on different mediums. On wort agar, for example, the wall of the cell remains thick and, in fact, becomes thicker with age.

With P. cerebriformis as with P. brasiliensis, there are formed terminal and intercalary chlamydospores, conidia, hyphal enlargements and sclerotic cells. In mature or old cultures the structure is markedly different from that of P. brasiliensis. The mycelia are in general much larger in diameter than those of P. brasiliensis. Filaments have a diameter of 2-7μ as contrasted with 1.5-3.5μ for the former. There are many more hyphal swellings; the chlamydospores are larger, as are the conidia, the terminal cells and the accessory cells. The hyphal cells are shorter and thicker, as contrasted with the elongated structures of P. brasiliensis (fig. 10). The cells here, furthermore, are arthrosporous, oidioid and dumbbell-shaped (fig. 10, *5, 9* and *11*). The chlamydospores are spherical, elongate, piriform or sclerotic and intercalary, lateral or terminal and range up to approximately 15μ and occasionally larger. The conidia are lateral, spherical or piriform and 3-10μ in diameter.

The formation of a large number of arthrospores, oidioid cells and chlamydospores which eventually are set free results in an abundance of isolated cells in old cultures. These take on various sizes and forms, so that on wort agar, as mentioned previously, the walls become thickened to such an extent that they appear as capsules from which a thick-walled cell may eventually slip out (fig. 10, *1* and *2*). This is a peculiarity of wort agar and of malt extract agar, mediums made up with an excess of carbohydrate, which probably explains the capsule formation. On other carbohydrate mediums, such as Sabouraud's agar (dextrose or maltose), in which the carbohydrate content is small or in which there is no glycerin, the filaments are somewhat finer.

Macroscopically, when grown on agar substrates, the colonies appear cerebriform, vermiculate or somewhat verrucoid, this being particularly evident on peptone agar, with the cerebriform appearance predominating. Subcultures on various other mediums do not markedly change this characteristic. The colonies are yeastlike, somewhat dull and easily separated from the substratum but are filamentous, flat, somewhat powdery and adherent to the dry portions of the agar slant. The colonies here, as with P. brasiliensis, are small, rarely attaining

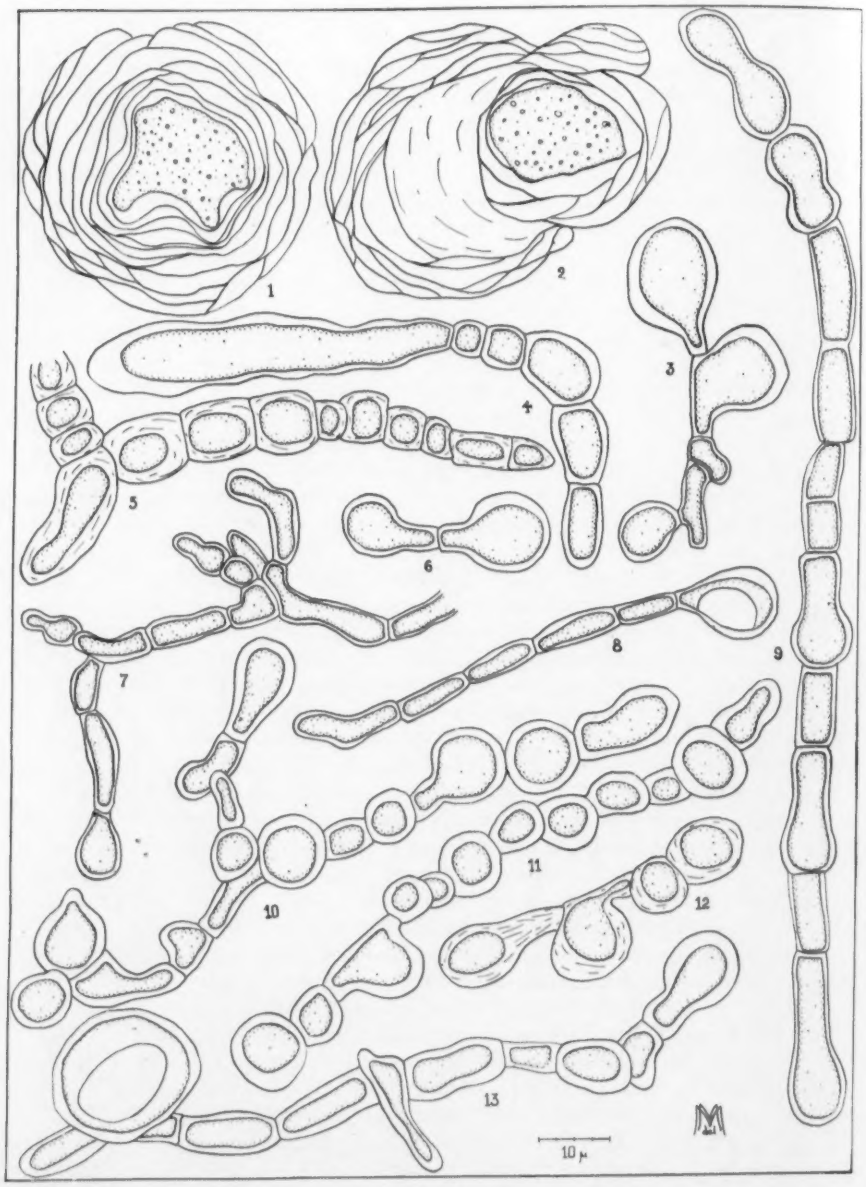


Fig. 10.—P. cerebriformis. All the drawings were made with the aid of a camera lucida at a magnification of × 1,960 and reduced. Parts *1* and *2* show large, thick-walled and encapsulated cells on wort agar; *3*, cells on malt extract agar; *4* and *5*, filaments of cells on wort agar; *6* and *8*, mycelium on Czapek's agar; *7*, cells on Sabouraud's maltose agar; *9*, a filament on peptone agar; *10* and *12*, mycelium on malt extract agar; *11*, cells on malt extract agar; *13*, a filament on peptone agar with an intercalary spherical cell.

or exceeding a diameter of 3 cm. The color of the colony varies from a creamy buff in the young stage to a light cinnamon buff in older stages.

Paracoccidioides tenuis Moore, sp. nov.

Cellulae in hospite, diametro 1-30μ paucies maiorae; gemmae singulae vel multae; cellulae sphericae vel ovoideae. In mediis diversis differt ab P. brasiliensis in magnitudine hypharum, cellularum, oidiorum, chlamydosporarumque. Hyphae septatae, ramosae, 1-3.5μ diametro. Cellulae sphericae, 5-20μ diametro; cellulae scleroticae, $5 \times 7 = 15 \times 20\mu$; oidia intercalaria ad 10μ diametro; chlamydosporae 4-10μ, circiter 5μ, sed ad 10μ; hyphae cum crescentibus circiter 4μ; hypnosporae terminales, circiter $7 \times 12 = 7 \times 25\mu$. Conidia lateralia, sessilia vel pedicellata, circiter 5μ. Culturae in mediis diversis bene crescent, sed male in Czapek's agar. Mycelium submersum, compactum. Culturae verrucoideae, vermiculatae, cerebriformes aut umbilicatae. Color albus vel subalutaceus. Fermentatio nulla. Lac non concretum, acidus nullus. Gelatinum non fluidificans.

When seen in tissue or in pus, this organism has all the characteristics found in P. brasiliensis, the cells being spherical or ovoid and 1-30μ in diameter and showing simple or multiple budding of minute, spherical, ovoid or bacillary gemmules of approximately 1μ and larger. When grown artificially it corresponds structurally to P. brasiliensis, except that the analogous structures are smaller proportionately (fig. 11). The hyphae are septate, branching and 1-3.5μ, in general being 1-2μ long; the spherical cells are 5-20μ in diameter, with sclerotic cells 5×7-$15 \times 20\mu$; the intercalary, oidioid cells range up to 10μ in diameter; the chlamydospores are 4-10μ, in general approximately 5μ but occasionally 10μ long; the hyphal swellings are of approximately 4μ; the terminal hypnospores usually range up to $7 \times 12\mu$ and occasionally up to $7 \times 25\mu$; the conidia are lateral, sessile or pedicellate and of approximately 5μ; racquet mycelium is present. Growth on artificial mediums in general is good but slow; it is poor on Czapek's agar. The colonies show mostly submerged mycelium, compact, verrucoid, vermiculate and somewhat cerebriform at inoculation, with a raised to umbilicate central portion, showing folds or radiating ridges. The color is white or that of the substratum, becoming light tan with age. Carbohydrates are not fermented; gelatin is not liquefied, and litmus milk is not curdled.

COMMENT

There are several factors which play an important part in this disease of South America and which consequently should not be overlooked. In the first place, I recognize clearly that paracoccidioidal granuloma as a disease entity is different from any other condition induced by pathogenic fungi, even though the difference may be slight in some respects. In the second place, the naming of the disease is a matter which merits a little attention. The name created by de Almeida came as a result of his establishing the genus Paracoccidioides, since a number of points were brought up by numerous authors to associate this group of organisms with C. immitis. The series of publications by de Almeida, however, definitely showed that the two disease processes were distinct and separate. Consequently, Jordon and Weidman,[8] with de Almeida's work as a basis, would call the South American disease de Almeida's disease. Although I am greatly in favor of honoring

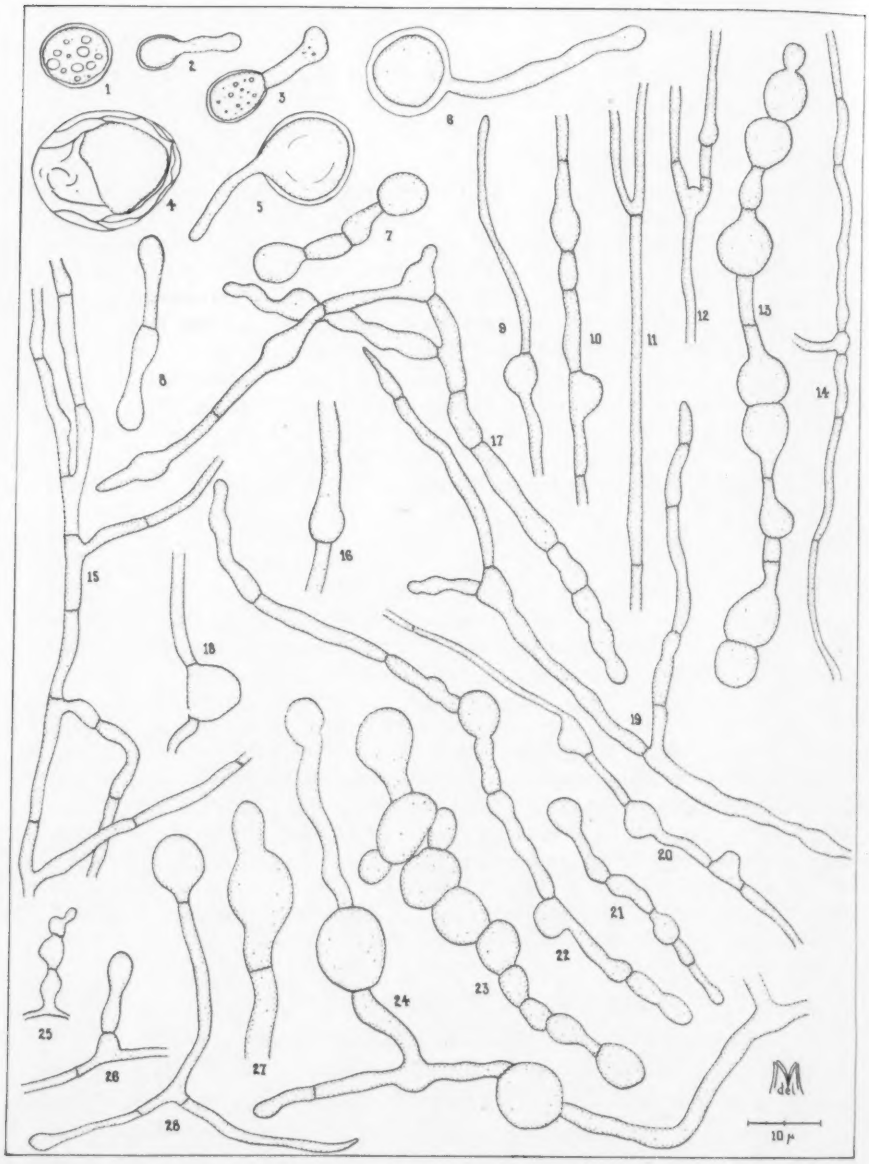


Fig. 11.—P. tenuis. All the drawings were made with the aid of a camera lucida at a magnification of × 1,960 and reduced. Parts *1* and *2* show germinating cells on wort agar; *3, 4, 8* and *13*, cells on malt extract agar; *5* and *6*, germinating cells on peptone agar; *7*, cells on wort agar; *9, 11* and *12*, hyphae on Czapek's agar; *10* and *14*, hyphae on Sabouraud's dextrose agar; *15*, a branching hypha on wort agar; *16*, a portion of racquet mycelium on peptone agar; *17, 19* and *26*, mycelium on glycerin agar; *18* and *20*, intercalary chlamydospore formation on Sabouraud's dextrose agar; *21*, a young filament on wort agar; *22*, a filament on malt extract agar; *23*, oidioid cells on malt extract agar; *24*, a branching hypha with intercalated swellings on peptone agar; *25*, a branch of cells on peptone agar; *27*, a terminal hypnospore on peptone agar, and *28*, a young branching filament arising from a cell on Sabouraud's agar.

a man for his work, even in such a small measure, yet there are several matters to be considered here. In the first place, a denomination such as this would indicate that the investigator whose name the disease bears was responsible in great measure for its demonstration and elucidation. A revision of the literature shows that paracoccidioidal granuloma as such was carefully pointed out by three men, Lutz, Splendore and Carini, years before de Almeida entered the field. With all due respect, of course, to the fine publications of de Almeida, who definitely proved that South American blastomycosis differed distinctly from coccidioidal granuloma, I find that all the characteristics emphasized in the present day publications were pointed out by these other authors, particularly by Splendore. As shown earlier in this paper, Splendore was able to distinguish two clinical types of the disease. Although his publications were not couched in present day mycologic language, his works bear all the earmarks of careful investigation. Therefore, the efforts of the older investigators must not be disregarded in such an important matter. If any personal nomenclature is to be used here, it should be, in the light of this knowledge, "Lutz-Splendore-de Almeida disease," a term to which de Almeida [34] seemed more inclined. However, for the benefit of future students, I am in favor of using more descriptive terminology, of leaving de Almeida's designation, paracoccidioidal granuloma, as the sole term for this disease.

The botanic classification of the fungi has involved some confusion, particularly with reference to C. immitis, the causative agent of coccidioidal granuloma. It has been supposed that the organisms of the two diseases present a number of similarities in tissue which could make differentiation extremely difficult. That, however, is not the case. The microbes in tissue and in pus are of completely different structure and life cycle, as was pointed out in the early part of this paper. On this basis it is sufficient botanically to classify these fungi in different categories. The generic determination is relatively simple, but the next problem is the designation of the family to which these organisms should belong. In a paper published in 1932 [13] the new designation Coccidioides esferiformis was established for P. brasiliensis, on the assumption that the description of the organism given to it by the South American investigators was correct. The fungus was then placed in the family Coccidioideaceae. The realization later that the term esferiformis had been used previously as a synonym for immitis ruled out this combination, with the result that de Almeida's genus was then considered as of equal generic rank with Coccidioides.[35] Ciferri and

34. de Almeida, F. P.: Personal communication to the author.

35. Moore, M.: A Morphological and Physiological Study of Two Species of Posadasia, Ann. Missouri Botan. Garden **22**:335, 1935.

Redaelli, however, created the new family Paracoccidioidaceae [36] for the single species P. brasiliensis that they examined. This family was placed in equal standing with Coccidioideaceae, which according to them is closely related to the families Olpidiaceae and their newly created Rhinosporidiaceae on the one side and Hyphochytriaceae on the other, all being placed in the order Chytridiales. The family is placed, therefore, in an isolated position near Rhizidiaceae, as a direct offshoot of Amoebochytrium, with the genus Catenaria of the family Cladochytriaceae following next in line. The space is too limited here for a complete botanic discussion of phylogeny and nomenclature. The fact, however, that the biologic phenomena of reproduction manifested in the multiple budding process in tissue were misinterpreted as endospore formation immediately rules out the line of reasoning and classification established by these authors. Until more exact knowledge is obtained, I should prefer that the genus Paracoccidioides remain in the family Coccidioideaceae, in equal standing with Coccidioides.

The nomenclature of the organism or organisms responsible for European blastomycosis is somewhat confusing. Busse in his publication referred to a "Saccharomycosis hominis," the fungus of which was termed Cryptococcus hominis by Vuillemin in 1901.[37] Since that time the fungi isolated in cases of European blastomycosis have been generally referred to by this denomination. In 1909 De Beurmann and Gougerot [28] established the genus Atelosaccharomyces, using Busse-Buschke as a species name for the same organism. This generic determination was followed by Dodge's [38] distinction of the genus from Cryptococcus on the basis of the fact that fermentation is present in Atelosaccharomyces and lacking in Crytococcus.

According to Busse's description of the fungus, dextrose and levulose are fermented, in which case the organism would be placed under Atelosaccharomyces. A number of publications since Busse's work have attributed to the isolated organisms various biochemical properties and morphologic characteristics which make their proper classification a little difficult. In the United States an organism supposedly similar morphologically and biochemically to the European microbe producing lesions of the brain and the meninges was first named Torula histolytica by Stoddard and Cutler. This organism now has generally been accepted as Cryptococcus histolyticus. Reports from such European investiga-

---

36. Ciferri, R., and Redaelli, P.: Paracoccidioidaceae, N. Fam., istituta per l'agente del "Granuloma Paracoccidioide," Bol. d. Ist. sieroterap. Milanese **15**: 97, 1936.

37. Vuillemin, P.: Les blastomycètes pathogènes, Rev. gén. d. sc. **12**:732, 1901.

38. Dodge,[2] p. 342.

tors as Lodder [39] and Giordano,[40] based on comparative studies of the various known existing yeastlike fungi of these groups from the United States and Europe, seem to indicate to them that these organisms all belong to one genus, Torulopsis, and to the species neoformans, described by Sanfelice in 1895.[41] The Torulopsis of these authors, however, was created in 1894 by Berlèse, who used as his type species Torulopsis rosea. To this genus then are referred the fungi which produce a pink or reddish pigment, a system followed by Dodge. Ciferri and Redaelli [42] replaced the type species with Torula gelatinosa and then used the genus to cover a number of cryptococci.[43]

If the work of these writers is correct, then it would seem that the term Torulopsis neoformans (Sanfelice) Redaelli should be used for the agent of European blastomycosis. However, further corroboration of the biologic phenomena is needed. This was carried out on a few strains by Benham.[44] Secondly, one is not certain as to the authenticity of several of the existing strains, which makes further proof difficult. Thirdly, the accepted usage of the term Cryptococcus hominis for the European pathogens makes it difficult to substitute another term, while C. histolyticus, as applied to the fungus producing torulosis [45] in the United States, seems to have a certain invasiveness which is not always demonstrated by the European microbes. On the other hand, it is possible that these yeastlike fungi may be identical, but a more intensive study is necessary to clear this matter up completely.

---

39. Lodder, J.: Die Anaskosporogenen Hefen. Erste Hälfte. Die Hefesammlung des "Centraalbureau voor Schimmelcultures," Beitrag zu einer Monographie der Hefearten 2, Amsterdam, 1934.

40. Giordano, A.: Rôle du "Torulopsis neoformans" (Sanfelice) Red. en pathologie humaine, Soc. internaz. di microbiol., Boll. d. sez. ital. **7**:119 (April) 1935.

41. Sanfelice, F.: Ueber einen neuen pathogenen Blastomycetin, welcher innerhalb der Gewebe unter Bildung kalkartig aussehender Massen degeneriert, Centralbl. f. Bakt. **18**:521, 1895.

42. Ciferri, R., and Redaelli, P.: Studies on the Torulopsidaceae, a Trial General Systematic Classification of the Asporogenous Ferments, Ann. Mycol. **27**:243, 1929.

43. Redaelli, P.: Le problème des torulopsidaceae et de leurs rapports avec l'homme et avec la pathologie humaine, Riv. di biol. **13**:171, 1931. Redaelli, P., and Cifferi, R.: A propos de nouveaux synonymes probables de Torulopsis neoformans (Sanf.) Red. 1931, Soc. internaz. microbiol., Boll. d. sez. ital. **7**: 243 (July) 1935.

44. Benham, R. W.: The Fungi of Blastomycosis and Coccidioidal Granuloma, Arch. Dermat. & Syph. **30**:385 (Sept.) 1934.

45. Mook, W. H., and Moore, M.: Cutaneous Torulosis, Arch. Dermat. & Syph. **33**:951 (June) 1936.

SUMMARY

This paper is best summarized as a brief description of the clinical aspects of the blastomycoses and of coccidioidal granuloma occurring in several localities, Europe, North America and South America; a description of the several fungi in tissue or pus and in culture, macroscopically and microscopically, and an epitome of the respective biologic phenomena, as seen in tables 1 and 2.

TABLE 2.—*Biochemical Reactions of North American, South American and European Organisms*

Reactions	Coccidioides immitis	Zymonema dermatitidis, Z. capsulatum, Z. capsulatum, var. Isabellinus	Cryptococcus hominis (?), Atelosaccharomyces hominis (?), (Torulopsis neoformans)	Paracoccidioides brasiliensis	Paracoccidioides tenuis	Paracoccidioides cerebriformis
Carbohydrates: Adonite Amygdalin Arabinose Dextrin Dextrose Galactose Inulin Lactose Levulose Maltose Mannitol Mannose Raffinose Rhamnose Saccharose Xylose	No fermentation or acidification	No fermentation or acidification	A. hominis (?) ferments (?) dextrose and levulose C. hominis (?) no fermentation Acidifies: dextrose galactose levulose maltose mannose saccharose C. histolyticus (?), no fermentation, acidifies the above	No fermentation or acidification	No fermentation or acidification	No fermentation or acidification
Litmus milk	Acid after five days marked with curdling on tenth day	No acid or curdling	No curdling, no acid or weakly acid	No acid or curdling	No acid or curdling	Acid starting sixth day; no curdling
Gelatin	Liquefaction in twenty-one days	Slow liquefaction beginning after approximately thirty days	Slow liquefaction with C. histolyticus after nineteen days No liquefaction (?), with C. hominis	No liquefaction	No liquefaction	No liquefaction

BOWEN'S DISEASE WITH METASTASES

(EPITHELIOMA OF BOWEN)

E. KUZNITZKY, M.D.
Formerly Director of the Skin Clinic of the Allerheiligen Hospital
IN COLLABORATION WITH
H. JACOBY, M.D.
BRESLAU, GERMANY

Since the extensive publications of Bowen,[1] Darier,[2] Jessner,[3] Arzt,[4] Arzt and Biach [5] and Ducrey,[6] a great number of cases of Bowen's disease have been published. It should be stated that usually Bowen's disease is harmless and benign, in spite of the general supposition that it is a definite precancerosis, that is, a disease in the course of which a formation of genuine tumors and metastases takes place "without exception and with certainty" (Beck [7]). The relative benignity has led Arzt and Biach [5] to express the belief that real Bowen's disease does not form metastases. There are, however, rare cases in which genuine metastases in the regional glands and in the internal organs occur. If one follows Darier's opinion that the typical histologic picture has to be found in the metastases, there remain only few cases belonging to the group in which malignancy has been proved beyond doubt.

Among the cases published before 1933, there were 3 of Darier's [2a] in which metastases were present in the adjacent regional lymph glands, while in only 1 case (Darier's third case) were there metastases in glands and organs at a distance from the original site.

REPORT OF A CASE

We are able to add to Darier's [2a] third case 1 which was briefly presented by Jacoby [8] at a meeting of the Silesian Dermatological Society in Breslau, Germany, on Feb. 20, 1930.

A 54 year old man was admitted to the roentgenologic department of the Allerheiligen Hospital in November 1929 for roentgen treatment of an ulcerated

1. Bowen, J. F.: J. Cutan. Dis. **30**:241, 1912; **33**:787, 1915.
2. Darier, J.: Ann. de dermat. et syph. (*a*) **5**:449, 1914; (*b*) **1**:49, 1920.
3. Jessner, M.: Arch. f. Dermat. u. Syph. **134**:361, 1921.
4. Arzt, L.: Zentralbl. f. Haut- u. Geschlechtskr. **30**:554, 1929.
5. Arzt, L., and Biach, M.: Arch. f. Dermat. u. Syph. **148**:635, 1925.
6. Ducrey, C.: Zentralbl. f. Haut- u. Geschlechtskr. **10**:268, 1924.
7. Beck, C. S., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 2, pt. 3, p. 433.
8. Jacoby, H.: Zentralbl. f. Haut- u. Geschlechtskr. **38**:440, 1931.

inoperable growth of the left groin. In September 1922 or 1923 there had been removed from the right umbilical region and from the inner side of the left thigh tumors which at that time had been considered angiofibromas. Histologic examination, however, had not been made. The tumors were said to have started to grow about ten years before. In April 1925 the patient consulted the physician who had operated. The right inguinal region showed an apple-sized tumor, which was not movable and was not associated with swelling of the regional lymph glands. A small nodule in the right costophrenic angle was barely movable. Histologic examination of the tumor, made by Professor Henke in the Pathological Institute of the University of Breslau, showed an infiltration with strands and nests of large epithelial cells and an abundance of mitotic figures, clumping cells and necroses. The diagnosis was squamous cell epithelioma. We feel that the histologic observations were typical of Bowen's disease at that time. Examination

Fig. 1.—Ulcerated tumor of the left groin.

of the patient in 1929 showed, in the left groin, a deeply ulcerated oval tumor, which was larger than a fist (about 10 by 7 cm.), and gave the impression of a cancerous lymph gland. The border of the tumor was elevated, bulged outward and showed hard infiltration. The base of the ulcer was covered with ill smelling, grayish black sloughs (fig. 1). The infiltration extended about 2 cm. beyond the border.

Examination of the rest of the skin showed in both supraclavicular fossae and along the left side of the chest circinate lentil-sized flat lesions, some of which formed larger serpiginous areas through coalescence (fig. 2). The lesions were partly covered with greasy crusts of a dirty brownish yellow. The area on the left side of the chest was 4 cm. in diameter and bean shaped. Removal of the crusts showed a surface which bled easily and which was raised only slightly above the surrounding skin.

Microscopic Examination.—The diagnosis of Bowen's disease, probable on clinical grounds, was confirmed by histologic examination of the cutaneous lesions. All the characteristics of this disease were found: broadening of the whole epidermis, parakeratosis, intercellular and intracellular edema and irregularities in

shape, size and structure of the cells and of their nuclei, with formation of giant cells and clumped nuclei (clumping cells). (*Corps ronds* and glycogen were not found.)

Histologic examination of the ulcerated tumor in the left groin showed strands of epithelium in coils and other characteristic features of Bowen's disease previously described (fig. 3). Glycogen was absent.

The interesting microscopic similarity between the tumor and the cutaneous lesions extended to the tumor of the right groin operated on in 1925. The Pathological Institute of the University of Breslau allowed us to reexamine the sections made then, and we could see that they represented metastases showing a mixture of epithelial and glandular elements.

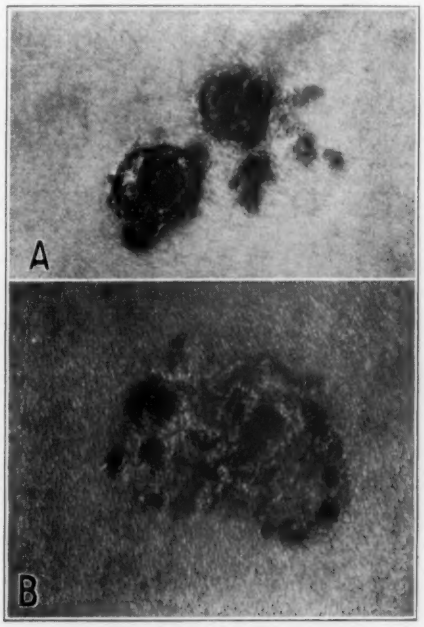


Fig. 2.—*A*, lesion of the supraclavicular fossa; *B*, lesion of the chest.

Subsequent Course and Treatment.—Electrodesiccation of the inguinal tumor followed by irradiation with mesothorium at a distance led to good results at first. The ulcer became much smaller; it finally showed almost complete epithelization and disappearance of the infiltration except at the upper border. The areas of cutaneous Bowen's disease were treated by contact irradiation with mesothorium (mesothorium carrier of 1 square centimeter, 21.33 mg. radium element equivalence, 1.5 mm. brass plus 0.1 mm. silver filter, two hours each area), which resulted at first in complete disappearance of the lesions. A small recurrence, which appeared three months later above the clavicles, was treated in the same way, after which the patient seemed to remain cured.

The good result obtained at the site of the inguinal ulcer did not last long, however. The patient began to have a high temperature, the cause of which could not be determined at first, until a large abscess perforated the middle of the tumor, which by this time had become widely ulcerated again. The abscess

led to a cavity extending deep into the pelvis. The infiltration of the outer edge increased again and, in spite of repeated intensive radium and roentgen irradiation, could no longer be stopped. The tumor grew deep into the pelvis, adhered to the sigmoid flexure and finally led to the formation of a stool fistula. Cachexia gradually became more severe; the patient finally died on Sept. 19, 1930.

Necropsy revealed that the tumor of the left groin extended down to the ilium. It was remarkable how easily it could be separated from the bone. Darier

Fig. 3.—Histologic section of the tumor (fig. 1).

observed the same phenomenon in his case. The sigmoid flexure was drawn toward the tumor and showed a sharply demarcated opening about 1.8 cm. in diameter. This was responsible for the discharge of feces through the abscess opening. The lymph glands along the abdominal aorta up to the diaphragm were filled with metastases. The right temporal bone showed two rough soft grayish red embedded lesions of about the size of a lentil without corresponding cutaneous lesions. The lymphatic glands of the right inguinal region were normal microscopically. Hypostatic pneumonia was present. The rest of the internal organs showed no abnormality.

Histologic Picture.—The tumor of the left groin showed multiple necroses and alterations of the epithelial structure, as already described. Glycogen was not seen. The periaortic glands showed a distinct Bowen structure of the epithelial strands in them, but there was much glycogen in places. The lymphatic glands of the right (surgically treated) groin showed nothing pathologic except a small dilatation of the sinuses (catarrh of the sinus). The areas in the right temporal bone which on gross inspection appeared to be metastases on histologic examination showed single cells in the bone marrow which had to be regarded as of epithelial origin, but these cells did not form a definite structure (syncytium). Unlike the cells in the periaortic glands, these cells were not differentiated enough to permit us to classify them as Bowen metastases.

COMMENT

The following lesions were found simultaneously: flat areas of the skin which did not yet show carcinomatous changes, a tumor with necrotic destruction which proved to be cancer, metastases in the periaortic glands and a glandular metastasis in the right groin which had appeared earlier than the tumor in the left groin. All these lesions revealed typical Bowen structure. However, the pathogenesis of the tumor in the left groin and that of the so-called metastases in the temporal bone were not established beyond doubt. The first had to be considered clinically as a glandular metastasis in the process of breaking down. In favor of this diagnosis were its location above Poupart's ligament, its size, its oval shape and the fact that a similar tumor at the same place had been diagnosed as adenocarcinoma. We considered as the primary focus the tumor on the inner side of the left thigh, which had been operated on in 1923. Such a location would permit metastases to either groin. The slow development of the tumor is a peculiarity of Bowen's disease; it certainly does not speak against it. Because of the involvement of the periaortic glands, the case is to be regarded as an instance of distant metastases. The microscopic picture being the same everywhere, it can be concluded that all these lesions belonged to the same nosologic entity, i. e., Bowen's disease. This brings up the question whether Bowen's disease invariably leads to cancer. Such a conception is held to be without basis by some authors, while others have doubts as to the type of cancer which eventually may develop from the lesions of Bowen's disease. Considering all these difficulties, we feel that we must subscribe to the views expressed by Mount [9] and Carol.[10] These authors wished to do away with the classification of Bowen's disease as a precancerosis; they expressed the belief that it should be termed an epithelioma of special structure (of the Bowen type). This opinion was confirmed by the findings in our case—so much so that we believe

9. Mount, L. B.: The Bowen Type of Epithelioma, Arch. Dermat. & Syph. **4**:769 (Dec.) 1921.

10. Carol, W. L. L.: Arch. f. Dermat. u. Syph. **152**:684, 1926.

we should make it our own. It has the great advantage of simplicity, and it makes possible the consideration of this difficult question in relation to allied diseases.

Histologically, Bowen's disease resembles squamous cell epithelioma through its cellular elements and through its peculiar way of growing, although it is sufficiently characteristic to be easily differentiated from true squamous cell epithelioma. As a matter of fact, it is one of the few dermatoses of which a diagnosis can be made through the microscope at first sight.

Since Krompecher's [11] and Darier's [2] famous investigations, which later were completed by J. Jadassohn's [12] final description, epithelioma of the skin has been distinguished according to the different cellular elements through which it has originated from the basal mother cell. According to its origin or according to its structure, it is referred to as basal cell or squamous cell epithelioma. The two kinds may be considered as the two ends of a continuous band, within which their two cells may be present in a given tumor in various combinations and permutations. At one side of such a band there would be "pure" basal cell epithelioma composed only of basal cells, with its variations, such as epithelioma terebrans; next would come the multicentric epithelioma of the trunk. These would be followed by the mixed forms: intraepidermal basal cell epithelioma (Borst and Jadassohn), Darier's metatypical epithelioma and the "mixed" form in which both mature basal and mature squamous cells are present. A transition form is known to exist in the "intermediary" type, in which the single cellular elements are not mature and therefore are neither typical basal nor typical squamous cells. This type has to be placed closer to squamous cell than to basal cell epithelioma, because the structure of the individual cells and their arrangement are more like those of squamous cells; this can be seen from the picture in W. Jadassohn's [13] publication. The intermediary epitheliomas would have to be placed, therefore, midway between the squamous and the basal end of the band. Analogous to intraepidermal basal cell epithelioma, an intraepidermal squamous cell epithelioma was to have been postulated to take the next place in the band. W. Jadassohn [13] found such a form only lately. The next places are occupied by Bowen's epithelioma and Paget's disease, both of which still possess the multicentric maternal soil but are able to make themselves independent of it. In the appearance of their single cells and in their structure they bear a considerable resemblance already to the squamous cell epitheliomas, although neither cell nor structure is mature. They occupy the

11. Krompecher, E.: Der Basalzellenkrebs, Jena, Gustav Fischer, 1903.
12. Jadassohn, J.: Beitr. z. klin. Chir. **26**:345, 1926.
13. Jadassohn, W.: Arch. f. Dermat. u. Syph. **171**:412, 1935.

place in the band opposite multicentric epithelioma of the trunk. Clinically the two can be mistaken for each other easily. The last place is then taken by the fully mature genuine squamous cell epithelioma.

One can group these epitheliomas not only according to their microscopic appearance but according to clinical facts, among which the degree of malignancy takes first place. It is known that the basal cell epithelioma—even its most severe representative, epithelioma terebrans—never forms metastases, while spinal cell epithelioma may do this relatively early. From our case and from the literature it is apparent that Bowen's and Paget's disease are the first links of a series of tumors which approach spinalioma in these clinical qualities. They take a similar position with regard to radiosensitivity; i. e., there is a decrease. While basalioma is sensitive to radiation, the intermediary forms show a progressive decrease of radiosensitivity as the slightly sensitive Bowen's disease is approached. Next in line is squamous cell epithelioma, well known for its lack of susceptibility to roentgen rays or radium. It is only by the most energetic treatment with a combination of surgical methods and the application of radon seeds and of roentgen rays that it can finally be cured.

The differentiation and classification of Bowen's disease has, we believe, a certain prognostic importance. The marked difference of this epithelioma from the squamous cell epithelioma is made evident by the fact that the Bowen metastases do not show cellular infiltration but simply push aside tissue, stopping in front of tissue of greater resistance, i. e., bone. They do not penetrate osseous tissue but simply grow alongside it. This increases the chances of success of operative procedures even in cases in which the involvement is extensive or would be considered inoperable otherwise.

SUMMARY AND CONCLUSIONS

A case of fatal Bowen's disease with metastases is presented. The patient was a 54 year old man, and the disease lasted probably from fifteen to seventeen years. From a tumor on the inner side of the left thigh the disease spread first to the inguinal glands and later to the periaortic glands. The skin of the supraclavicular fossae and of the left side of the chest showed typical Bowen lesions. Histologic examination of the cutaneous lesions and of the metastases revealed identical pictures. Bowen's disease should not be called a precancerosis but an epithelioma of special structure of the Bowen type. An attempt to place it histologically in its proper place with regard to other types of epithelioma of the skin links it pretty closely to squamous cell epithelioma, a fact which is borne out by such clinical evidence as its relatively slight radiosensitivity and its occasional tendency to form metastases.

Kaiser Wilhelmstrasse 29.

ARSENICAL DERMATITIS PRODUCED IN TREATMENT OF TRICHOMONAS VAGINITIS

REPORT OF FIVE CASES

BEATRICE M. KESTEN, M.D.
NEW YORK

Acetarsone and related compounds containing pentavalent arsenic are used with increasing frequency in the treatment of infections caused by Trichomonas vaginalis. It seemed of interest to report briefly four cases in which localized dermatitis followed the use of one of these compounds and in which the course, the appearance and the distribution of the eruption were strikingly similar. In a fifth case to be reported the dermatitis produced was generalized and indistinguishable from that produced by the arsphenamines.

REPORT OF CASES

CASES 1, 2 AND 3.—Three women with resistant trichomonas vaginitis received weekly or bimonthly treatments over periods of eight, ten and fourteen months, respectively. None gave a history of previous dermatitis or of treatment with arsenic. All received the insufflation treatment for infection due to Trichomonas with a preparation labeled "powdex—formula 21." The composition stated on the label was

	Grains	Gm.
Cinquarsen (acetarsone)	7½	0.48
Salicylic acid	1⅕	0.77
Zinc oxide compound and aromatics, q. s.	4	0.25

Indic: Trichomonas vaginalis.

No cutaneous symptoms were noted by any of these patients until at least twenty treatments had been received. At varying periods after this each noted a burning sensation about the vulva and the appearance of a fine red itching rash on the labia and the inner parts of the thighs. Within a few days a similar symmetrical rash was noted in the antecubital areas. In addition, a similar rash developed on the chin of one patient. In all these patients the eruption consisted of well circumscribed erythema in which there were innumerable macules and a few maculopapules.

From five to thirteen days after the treatment was discontinued the eruptions desquamated, leaving a normal-appearing skin. Two of these patients received one more insufflation of powdex, which produced a prompt recurrence of the eruption. A patch test with powdex applied to the antecubital area of one patient after the eruption had subsided did not reproduce the dermatitis.

From the Department of Dermatology, College of Physicians and Surgeons, and the Vanderbilt Clinic, Columbia University.

CASE 4.—A physician's secretary with trichomonas vaginitis received one treatment with powdex from a gynecologist. This produced improvement. Because she thought the cure might be hastened, she had the office nurse give her treatment every other day for ten days. On the day following the sixth treatment an acute erythematous macular eruption similar to those just described developed on the groins. The application of soothing lotions and of potassium permanganate soaks cleared this in two weeks.

CASE 5.—The fifth eruption occurred in a young mother shortly after the birth of her second child. Before her pregnancy she had received instillations of powdex for the treatment of an infection caused by Trichomonas vaginalis. After delivery her profuse vaginal discharge was not controlled by the usual measures, and as Trichomonas was still present she was given three more treatments with powdex at intervals of three or four days. Before any of these treatments the skin over the perineum, the groins and the anus was red, swollen and somewhat pruritic. After the first treatment this eruption grew worse, and a generalized itching rash appeared. This was controlled with epinephrine and calamine lotion. There was a similar flare after the second and after the third instillation of powdex. The last exacerbation did not subside with the previously described medication. The patient was first seen three days after the last instillation of powdex. At that time she had a generalized erythematous, papulovesicular eruption and rather marked edema of the face, particularly of the eyelids. The membranes of the mouth were dry and red, and the tongue was somewhat swollen. The patient complained of chilliness and of generalized burning itch. With discontinuance of the use of powdex and with soothing baths and local applications, the eruption slowly cleared.

COMMENT

These cases are examples of sensitization to a pentavalent arsenical following absorption through the vaginal mucous membrane. Sensitization occurred in four cases after prolonged moderate and in one after short intensive treatment. In one case severe generalized dermatitis indistinguishable from an arsphenamine dermatitis resulted from persistence in arsenical treatment after the first evidences of sensitization had appeared.

LEUKODERMA ACQUISITUM CENTRIFUGUM IN ASSOCIATION WITH LICHEN PLANUS

SAUL S. ROBINSON, M.D.
LOS ANGELES

Although leukoderma acquisitum centrifugum has usually been described in association with pigmented nevi, a survey of the literature reveals that this condition occurs with psoriasis,[1] senile verruca,[2] fibroma,[3] papular sarcoid [1] and vascular nevus.[4] Feldman and Lashinsky [5] have recently reviewed the literature and reported five cases in which leukoderma acquisitum centrifugum occurred in association with moles. For this association they suggested the name halo nevus. No report could be found in the literature of the occurrence of leukoderma acquisitum centrifugum in association with lichen planus. The following case is therefore believed to be of interest:

REPORT OF CASE

Mrs. H. F., aged 48, consulted me because of a generalized itching eruption which, she stated, had appeared suddenly about two months previously on the trunk and the extremities and had gradually spread. The pruritus was severe at times and interfered with sleep. There was no history of ingestion of medicaments.

The dermatologic examination revealed the trunk to be covered with small reddish blue, discrete and confluent, flat, angular papules typical of acute disseminated lichen planus. The eruption sparsely covered the upper and the lower extremities and involved especially the flexor surfaces of the forearms. Brownish pigmented relics of former papules were scattered over the back and the extremities. The mucous membranes of the mouth and the throat were normal. Of unusual interest in the eruption was a round, sharply defined area of depigmentation

---

From the Department of Dermatology, the Cedars of Lebanon Hospital.

1. Stokes, J. H.: Clinical Note on Leukoderma Acquisitum Centrifugum (Sutton), Arch. Dermat. & Syph. **7**:611 (May) 1923.

2. Petges: Leucoderma Acquisitum Centrifugum (Sutton), Dermat. Wchnschr. **80**:401, 1925. von Szentkirályi, S.: Die Strahlenempfindlichkeit des Leukoderma acquisitum centrifugum, Orvosi hetil. **70**:1411, 1926.

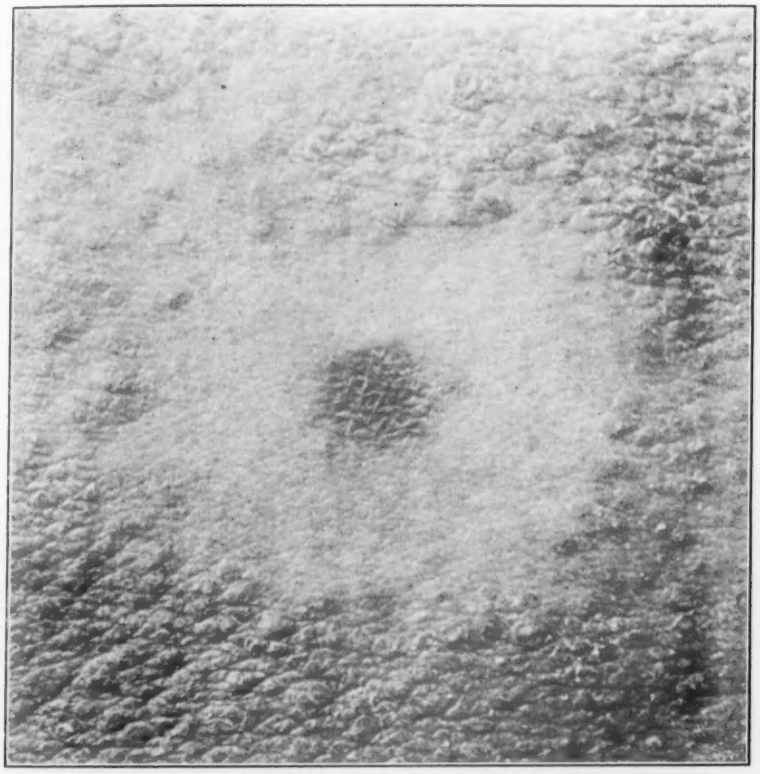
3. (*a*) von Leszczyński, R.: Ueber Suttonsche Krankheit (Leucoderma Acquisitum Centrifugum), Dermat. Wchnschr. **82**:575 (April 24) 1926. (*b*) Mgebrow, M. G., and Pridsky, I.: Vitiligo in der Umgebung von Naevi (Leukoderma Acquisitum Centrifugum—Sutton); Vitiligo périnaevique, Russk. vestnik dermat. **7**:338, 1929.

4. Katz, L.: Beiträge zur Kenntnis der Vitiligo, Dissert., Breslau, 1923.

5. Feldman, S., and Lashinsky, I. M.: Halo Nevus: Leukoderma Centrifugum Acquisitum (Sutton), Arch. Dermat. & Syph. **34**:590 (Oct.) 1936.

the size of a half-dollar on the right loin, surrounding a central pea-sized area of grouped, flat, brownish red papules. The border was not hyperpigmented. This depigmented lesion was entirely surrounded by papules of lichen planus, but none of these were present within its zone. The patient stated that the leukoderma acquisitum centrifugum had appeared at the time of onset of the generalized eruption and had become more pronounced since the eruption on the trunk had spread and surrounded the white area.

A biopsy specimen removed from the borderline of the central papular lesion and the surrounding depigmented area showed hyperkeratosis, a thickened stratum



Leukoderma acquisitum centrifugum in association with lichen planus (× 2)

granulosum, acanthosis and colliquative degeneration of the rete cells in the papular lesion. The borderline between the epidermis and the cutis was ill defined. The papillary and the subpapillary layer of the cutis presented a sharply demarcated infiltration of lymphocytes. Occasional clumps of melanin and chromatophores were scattered throughout the cutis. No nevus cells were present. The depigmented skin surrounding the papular lesion showed only occasional pigmented granules in the basal cells of the rete, with slight perivascular round cell infiltration in the papillary and the subpapillary layer of the cutis. There were no pathologic indications of lichen planus. The pathologic diagnosis was lichen planus and leukoderma.

COMMENT

Leukoderma acquisitum centrifugum has been considered by many investigators to be a variety of vitiligo. Reports [6] have been made of leukoderma acquisitum centrifugum accompanied with true vitiligo. The absence of papules of lichen planus within the depigmented portion of my patient's area of leukoderma acquisitum centrifugum and the spread of the surrounding papules of lichen planus stopping at the edge of the area of leukoderma, are of unusual interest because of the reports by Madden [7] and Walzer [8] of papules of lichen planus occurring in patches of vitiligo. In Madden's case pale papules of lichen planus of six months' duration were present in twelve year old patches of vitiligo on the wrists and the legs and absent in normally pigmented areas of skin. These observations indicate that true lesions of vitiligo and of lichen planus may coexist in the same cutaneous area. The depigmented region of leukoderma acquisitum centrifugum in my case, however, was free from the lesions of lichen planus although entirely surrounded by them. The difference in the behavior of lichen planus in relation to patches of true vitiligo and to the depigmented area of leukoderma acquisitum centrifugum indicates that there may be a different cause for the depigmentation of leukoderma acquisitum centrifugum and of vitiligo.

1930 Wilshire Boulevard.

6. Bunch, J. L.: White-Spot Disease and Vitiligo, Brit. J. Dermat. **30**:203 (Oct.-Dec) 1918. Siemens, H. W.: Leukoderma Acquisitum Centrifugum, Zentralbl. f. Haut- u. Geschlechtskr. **30**:15, 1929. Montpellier, J.: Vitiligo à début périnaevique, Bull. Soc. franç. de dermat. et syph. **29**:81, 1922. Narducci, F.: Sul nevo leucopigmentario e sulla vitiligine perinevica, Arch. ital. di dermat., sif. **1**:271, 1925. von Leszczyński.[3a] Mgebrow and Pridsky.[3b]

7. Madden, J. F.: Lichen Planus and Vitiligo (Lesions Appearing in Patches of Vitiligo), Arch. Dermat. & Syph. **30**:122 (July) 1934.

8. Walzer, A.: Lichen Planus Annularis and Vitiligo, Arch. Dermat. & Syph. **20**:418 (Sept.) 1929.

INCIDENCE OF DISEASES OF THE SKIN IN FEEBLEMINDED PERSONS

THOMAS BUTTERWORTH, M.D.
READING, PA.
AND
McCLELLAN WILSON JR., M.D.
SPRING CITY, PA.

Statistical surveys of the incidence of different diseases of the skin are influenced to a great extent by the age, the race and the social level of the subjects studied, as well as by the diagnostic interpretation of the examining physician. The seasonal variations which are noted in many diseases affect studies made within a short period. Further discrepancies occur when the cases recorded have been observed independently by two or more physicians. Such diversification is made evident by a comparison of the lists of the "ten most common cutaneous conditions" prepared by Lane,[1] by Goodman,[2] by Gilman [3] and by Alderson and Reich.[4] There are differences not only in the ten diseases composing the several lists but in their relative positions. Four diseases, dermatitis, pyoderma (including impetigo), acne vulgaris and tinea, appear in all four compilations. Eczema, urticaria, herpes (zoster and simplex), verrucae and seborrhea are found on three of the four lists. Psoriasis is included in two lists, while pruritus, scabies, alopecia, pityriasis rosea, moles, sebaceous cysts and pediculosis pubis are noted in one.

Even though the present survey concerns, as do many previous reports, the observations on a special class of subjects, it differs in that a large group was systematically studied, irrespective of whether the individual members complained of a cutaneous disorder. When persons are privileged to seek medical attention, it would seem that the more annoying diseases would be accorded a higher incidence than relatively symptomless diseases. The entire population of the Pennhurst State School for the Feebleminded, comprising 1,895 patients, of whom 1,062

1. Lane, C. G.: The General Practitioner and His Work, A. M. A. Bull. **24**:100 (April) 1929.

2. Goodman, H.: Statistics of Ten Most Common Skin Diseases, Based on Analysis of 973,090 Cases, Arch. Dermat. & Syph. **20**:186 (Aug.) 1929; Tinea: Second Most Prevalent Disease of the Skin, ibid. **23**:872 (May) 1931.

3. Gilman, R. L.: Incidence of Skin Diseases in a Student Health Service, Am. J. M. Sc. **188**:268 (Aug.) 1934.

4. Alderson, H. E., and Reich, A.: Incidence of Dermatoses in a Student Health Service, Arch. Dermat. & Syph. **36**:57 (July) 1937.

(56 per cent) were male and 833 (44 per cent) females, was examined in the spring of 1935. There were 1,834 (96.8 per cent) white subjects and 61 (3.2 per cent) Negroes. Seventy-two per cent of the patients were between the ages of 10 and 30 years, the distribution according to age being as follows: first decade, 7 per cent; second decade, 42 per cent; third decade, 30 per cent; fourth decade, 15 per cent; fifth decade, 4 per cent; sixth decade, 1 per cent, and beyond the sixth decade, 1 per cent. The majority of the patients were from urban centers, such as Reading, Pa., Scranton, Pa., and Philadelphia.

The skin and the accessible mucous membranes were systematically studied. All patients were examined when naked. A certain amount of resistance was encountered in inspecting the throats of a few of the patients with lower grades of feeblemindedness; and physical difficulties, in studying all the cutaneous surface of the crippled patients. For the

Ten Most Common Cutaneous Diseases at the Pennhurst State School for the Feebleminded

	Number of Cases
Acne vulgaris	152
Nevi	140
Tinea	63
Pyoderma	53
Striae distensae	39
Dermatitis traumatica	30
Verrucae	20
Hypertrichosis	17
Perleche	16
Molluscum contagiosum	16

most part, the patients cooperated well, since they were accustomed to frequent examinations by the house staff and were intrigued by the change in routine.

There were 780 dermatologic diagnoses made in 654 cases. The incidence of cutaneous diseases and abnormalities was about equal in the two sexes. A total of 68 different dermatologic conditions was observed. Of the total number of diagnoses, 546, or 70 per cent, were of one of the ten most common conditions, listed in order of frequency in the table. Seborrhea just missed the list, with 15 cases, and was closely followed by scabies, with 14 cases.

Acne vulgaris was the most common condition, as might have been expected from the age of the patients studied. The incidence of this disease was almost exactly equal in male and in female subjects. As no attempt was made to classify the various types, it is probable that in a number of cases mild acne was overlooked.

Many varieties of vascular and nonvascular nevi were noted. Multiple pigmented nevi comprised the largest group of the latter type; but non-pigmented, hairy, comedone and giant forms were also recorded. Representative examples of each of the several groups of vascular nevi were observed, as well as mixed types. As with acne vulgaris, we feel that a certain number of cases of nevi were overlooked, particularly solitary pedunculated nevi spili.

Under the classification "tinea" (or ringworm) were placed fungous infections of the toes, the hands, the groins, the body, the scalp and the nails, pompholyx and tinea versicolor. Of the total of 63 cases falling within this group, 34 were cases of tinea versicolor. This disease exhibited a suggestive epidemiologic distribution, in that 18 affected patients lived on one of two floors of one cottage for men and 16 in one cottage for women. Isolated patients with tinea versicolor were not found. In 5 cases ringworm of the scalp was noted. Prompt isolation probably prevented a higher incidence.

One of the most surprising features of the survey was the remarkably low incidence of ringworm of the feet. In only 14 cases, or less than 1 per cent, was there clinical evidence of such infection. The institution uses no antiseptic foot baths to prevent this infection, but the condition is treated effectively as soon as it is discovered. Possibly the most important factors in preventing its spread are the frequent bathing of the patients under proper supervision and the equally regular scrubbing of the floors of the shower rooms and dormitories.

Pyoderma is a term used for all the simple forms of pyogenic dermatitis, including impetigo, furuncle, secondary infections and ecthyma. Feebleminded persons often injure themselves either by accident or by picking themselves during periods of agitation. Since they seem to have a lowered resistance to pyogenic organisms, minor abrasions are frequently followed by infection. The patients spread the disease and prolong the infection by picking the lesions. The hygienic measures that seem so effective in limiting ringworm do not apparently prevent the occurrence of pyoderma.

Striae distensae were noted in 39 persons, almost all of whom were adolescent girls. In 30 of the patients there had been a rapid gain in weight and in 9 a loss of weight since admission. No information as to whether the atrophic striae occurred before or after the loss of weight in the latter group was available. Although many of the patients were agitated and underweight on admission, they soon adjusted themselves to institutional routine and rapidly became heavier. Pituitary and thyroid manifestations were suggested in some, but no analysis was attempted

along this line. This condition, because of its asymptomatic nature, would hardly be expected to occur among the ten most common cutaneous diseases in clinical or private practice.

Under the term dermatitis traumatica we have included a condition seldom seen in ordinary practice. Patients with mental disease injure themselves when annoyed or tormented by violently biting their hands and wrists. The skin in these regions becomes erythematous, thickened, dry and hyperkeratotic (fig. 1 *A*). Frequently the keratotic thickening

Fig. 1.—*A*, erythematous hyperkeratotic plaque, resulting from frequent biting of the hand; *B*, circinate hyperkeratotic plaque, corresponding with the shape of the alveolar processes, caused by the patient's constant biting in the same place.

occurs in a circle representing the size and the shape of the configuration of the patient's teeth (fig. 1 *B*). These patches persist indefinitely, being further irritated by repeated biting. Ordinarily, patients with mental disease bite or pick the same parts all the time, in contrast to neurotic persons, who frequently excoriate widespread portions of the body. In most instances, a callous-like hardness occurs, but an atrophic scar is

seen occasionally (fig. 2). In the more common hypertrophic type of involvement it would seem that the pressure has been comparatively slight and often repeated, while in the atrophic type the trauma has been greater, and actual lacerations have been produced. A section from the hand of a patient with a hypertrophic lesion showed marked thickening of the epiderm, hyperkeratosis and hyperplasia of the collagenous material.

Common warts occurred in 17 patients and the flat juvenile type in 3. In every instance the lesions were multiple. No plantar warts were found.

An excessive growth of hair on the face and the body was observed in 12 male and 5 female patients. Marked hypotrichosis was noted in

Fig. 2.—Atrophic scars following repeated biting of the hand.

1 man. Among the more common abnormalities of growth recorded were low hair lines and fusion of the eyebrows. Abnormal distribution of the pubic hair was likewise frequently seen.

Perlèche ranked as the ninth most common cutaneous disorder. Because many patients with mental disease drivel constantly, the skin about the corners of the mouth is more or less continually wet. Secondary fissuring is frequent. Almost all the cases noted occurred in young children.

As there was an outbreak of molluscum contagiosum in one of the cottages at the time the survey was made, 16 cases gave this disease a place among the ten most common diseases of the skin. Ordinarily, we feel that seborrhea would occupy a place on the list. The comparative infrequency of seborrheic processes is probably related to the practice

of cutting the hair close to the scalp and of frequent washing of the head. This same custom may account also for the complete absence of head lice in the group studied.

For conditions not already mentioned but included in other compilations of the ten most common cutaneous diseases, we noted the following incidence: eczema (true allergic) in 2 cases, urticaria in 3, herpes (simplex and zoster) in 4, psoriasis in 3, alopecia (areata and cicatrisata) in 2, pediculosis pubis in 1 and sebaceous cysts in 8.

Five cases of neurofibromatosis were noted. Typical subcutaneous and cutaneous nodules, together with "café au lait" spots, were exhibited. If, however, we classify all those cases in which there are simply "café au lait" spots as cases of early or abortive Recklinghausen's disease, then that condition assumes a high rank among the most common cutaneous diseases, with a total of 55 cases. As it is well known that the coffee spots frequently antedate the occurrence of tumors, it will be interesting to watch the future course of these patients.

Six patients exhibited the cutaneous manifestations of adenoma sebaceum. All of these were epileptic. Extensive clinical and histologic studies, which will form the basis for a later report, were made on this group.

The encephalotrigeminal syndrome was definitely proved in 1 patient and was probably present in 2 others. This syndrome is characterized by the occurrence of angiomatosis of the brain, associated with cutaneous nevi in the area of trigeminal distribution. The affected persons showed progressive mental deterioration, with increasingly frequent epileptic seizures. In the case in which the diagnosis was established the presence of a calcified angioma of the brain was demonstrated by means of a roentgenogram.

Another common nevoid change was scrotal tongue. The degree of fissuring varies so much that it is frequently difficult to state whether in a given case the tongue is normal or mildly scrotal. In approximately 6 per cent of our cases there was some thickening and fissuring. The condition was noted particularly in idiots, in whom it often begins between the third and ninth month but occasionally not until the second year.

Vasomotor changes were commonly noted but were difficult to record statistically. Many of the patients presented a constant, cold bluish redness of the hands and the feet, varying from a mild discoloration to considerable change. The parts were often wet with sweat. These changes in color were more pronounced in cold weather. Such vasomotor changes have been described as acrocyanosis or chronic acroasphyxia. It is not unlikely that a poorly adjusted vegetative nervous system is unusually frequent in patients whose admission to an institution for feeblemindedness depends on inferior nervous tissue.

Many stigmas were noted in the course of our examination. Irregularities in the size, the number and the position of the teeth were frequent. Hutchinson's incisors were found only in cases of known congenital syphilis, while mulberry molars occurred in 21, or slightly more than 1 per cent, of all patients. The external ear exhibited anomalies of form and size, as well as attachment of the lobe to the cheek. Saddle and v-shaped palates were numerous. Thyroid and pituitary disturbances were suspected in a number of cases, but no attempt was made to investigate these. Although disturbances of sexual characteristics were frequent, they did not lend themselves to ready classification and tended to lead away from the prime purpose of our study.

Among the remaining cutaneous diagnoses were a number of interesting or unusual conditions not related to mental disease. These conditions were too few to be of value from a statistical point of view but added greatly to the interest of the survey.

411 Walnut Street.

Pennhurst State School for the Feebleminded.

SCLEREDEMA ADULTORUM (BUSCHKE)

HARRY L. ARNOLD JR., M.D.
Resident in Dermatology and Syphilology, University of Michigan Medical School
ANN ARBOR, MICH.

In 1902 Buschke [1] reported an unusual case of hardening of the skin which he had presented before the Berlin Dermatological Society two and a half years before. No diagnosis had been made at the original presentation—indeed, none of the members present could recall having observed a similar case—but Buschke entitled his report "Ueber Scleroedem." The patient was a 46 year old carriage varnisher who, after an attack of influenza, had noticed stiffening of his skin, beginning on the neck and spreading to involve all of his body proximal to the thighs and the fingers. Buschke considered and discarded alternative diagnoses of scleroderma, myxedema, trichinosis, dermatomyositis, blood and lymph stasis and scleredema neonatorum. He chose the name *Scler-oedem*, or scleredema (not "sclero-edema," as it has sometimes been mistranslated), because of the resemblance of this apparently new entity to the last of the previously named conditions and added the qualifying "adultorum" to distinguish this type.

HISTORICAL REVIEW

Prior to Buschke's report at least ten cases of this disease had been described, one in 1752 by Curzio [2] and the remainder from 1845 to 1865 by other writers. These reports have been listed by Touraine and his associates.[3] None of them suggested, however, that the authors were aware that they were dealing with a hitherto unrecognized syndrome. Since 1902 approximately sixty cases have appeared in the literature; of this number only seven have been reported from the United States and three from France; the remainder have appeared in German and

---

Studies and contributions from the Department of Dermatology and Syphilology, University of Michigan Medical School, Service of Dr. Udo J. Wile.

1. Buschke, A.: Ueber Scleroedem, Klin. Wchnschr. **41**:955 (Oct. 15) 1902.

2. Curzio, C.: Dissertation anatomique et pratique sur une maladie de la peau, d'une espèce fort rare et fort singulière, translated from the Italian by M. V., Paris, chez Vincent, 1755.

3. Touraine, A.; Golé, L., Soulignac, L.: Sur l'historique du "Scléroedème de l'adulte" dit de Buschke, Bull. Soc. franç. de dermat. et syph. **43**:1842 (Dec.) 1936.

Austrian journals. Epstein [4] described the first two American cases in 1932; Guy and Amshel [5] in 1934 and Pillsbury [6] in 1935 presented two cases without reporting them; Frank [7] reported a typical case in November 1937, and Sweitzer and Laymon [8] added two more to this number. Their two cases were presented before the Dermatological Conference of the Mississippi Valley in September 1936 by Michelson and Laymon.[9] The case which prompts this report will be the eighth American case and the sixty-first to appear in medical literature. Buschke's choice of a name for the condition has been uniformly accepted by writers on this subject; the *Index Medicus,* unfortunately, has mistranslated it as "sclero-edema," but no article on it bears that title. Sellei [10] deplored the name as inapt and optimistically suggested the admirably descriptive but hopelessly unwieldy name induratio progressiva benigna sub cute.

ETIOLOGY

In most of the reported cases the condition has followed closely either an acute exanthem or an acute infection of the upper part of the respiratory tract. Mastoiditis, tonsillitis, parotitis and nephritis have been observed to precede immediately the onset of the condition. In our case the condition was preceded by tuberculous cervical lymphadenitis. In some cases the condition apparently has developed spontaneously in healthy persons. Women have been more often affected than men. There seems to be no significant age limit. The physiopathologic mechanism involved is not understood; most conjectures center around the toxic liberation of a mucin-like substance into the subcutaneous connective tissue.

CLINICAL COURSE

Little variation has been reported in the clinical picture. Stiffening and hardening of the subcutaneous tissue, described often as woody or cartilaginous and always as deep, develops in the back of the neck and

4. Epstein, N.: Scleredema Adultorum (Buschke), J. A. M. A. **99**:820 (Sept. 3) 1932.

5. Guy, W. H., and Amshel, F.: Scleredema, Arch. Dermat. & Syph. **29**:777 (May) 1934.

6. Pillsbury, D.: Sclerema (sic) Adultorum (Buschke), Arch. Dermat. & Syph. **32**:691 (Oct.) 1935.

7. Frank, L. J.: Scleredema Adultorum (Buschke), Arch. Dermat. & Syph. **36**:1052 (Nov.) 1937.

8. Sweitzer, S. E., and Laymon, C.: Scleredema Adultorum (Buschke), Arch. Dermat. & Syph. **37**:420 (March) 1938.

9. Michelson, H. E., and Laymon, C. W.: Scleredema Adultorum, Arch. Dermat. & Syph. **35**:960 (May) 1937.

10. Sellei, J.: Skeleroedema adultorum (Bushke): Induratio progressiva benigna sub cute, Dermat. Ztschr. **54**:161 (Sept.) 1928.

spreads by direct extension over the face, the arms and the trunk in a few weeks. Involvement of the legs has been seen only in children; involvement of the feet has not been observed at all. Most observers have confirmed Sellei's [10] dictum that the hands are invariably spared, but in Buschke's original case [1] and subsequently in cases reported by Maschkilleisson and Abramowitsch [11] and by Darier, Ferrand and Mircouche [12] involvement of the backs of the hands, extending as far as the fingers, was described. This apparently unusual distribution was likewise observed in our case.

The involved areas are stiff and firm to the touch; they look and feel somewhat edematous but cannot be made to "pit" on pressure. Sensation, pigmentation and perspiration are unaffected, and there is no pain. Atrophy does not occur, and changes in the bone, so common in cases of sclerodactylia, have not been described. Recurrence, years after the initial attack, has been described in four cases. The disease usually progresses for from two to six weeks and then regresses for a year or two, complete restoration to normal being the invariable rule.

DIFFERENTIAL DIAGNOSIS

The disease must be distinguished in infants from sclerema neonatorum, edema neonatorum and necrosis of the subcutaneous fat and in adults from dermatomyositis, trichinosis, diffuse scleroderma and myxedema. Briefly, scleredema does not present the change in color characteristic of the first two conditions named, the circumscribed lesions of necrosis of the subcutaneous fat, the pain or the superficial changes of dermatomyositis, the muscular tenderness or eosinophilia of trichinosis or the many characteristic concomitant changes in addition to the "false edema" of myxedema. There may be a little more difficulty in distinguishing it from the edematous phase of diffuse scleroderma, but it should soon be evident that the freedom from subjective symptoms (except stiffness), the absence of pigmentary changes, the absence of atrophy and, lastly, the freedom of the fingers from involvement militate strongly against a diagnosis of scleroderma.

HISTOLOGIC PICTURE

The histologic picture has been discussed in detail by Sellei [10] and Freund.[13] Briefly, it consists of swelling and separation from one

11. Maschkilleisson, L. N., and Abramowitsch, L. A.: Ueber Skleroedema adultorum Buschke, Dermat. Ztschr. **72**:283 (Dec.) 1935.

12. Darier, J.; Ferrand, M., and Mircouche: Sclérémie des adultes: Amélioration par le traitement thyroidien, Bull. Soc. franç. de dermat. et syph. **26**:172 (June 12) 1919.

13. Freund, H.: Histologische Befund bei Sklerödem (Buschke), Zentralbl. f. Haut- u. Geschlechtskr. **33**:303, 1930.

another of the bundles of collagen in the deeper layers of the corium, with an inconstant moderate infiltration of round cells about the dilated blood vessels and thickened nerves. Buschke and Ollendorff [14] have described a case in which the deeper fascia and muscles were the chief site of involvement, but this is by no means the rule. The epidermis in all cases appears unaltered. Many investigators have been able to stain a "mucin-like" substance lying in the interstices among the bundles of collagen.

TREATMENT

Baths, keratolytic measures, massage and oral administration of thyroid have been the most widely used therapeutic method. One writer expressed the belief that there was improvement attributable directly to thyroid therapy. No one else has suggested that any form of treatment hastened the spontaneous involution of the disease.

REPORT OF A CASE

G. S., a 15 year old girl of Slavic parentage, came to the University Hospital on July 8, 1937, complaining only of swelling of the glands of the neck. This had begun gradually in 1933; the glands had remained small, however, until 1935, when they began to increase in size. At that time she went to a Detroit hospital, where she received four doses of high voltage roentgen radiation over the right side of the neck, without improvement. This treatment was repeated in 1936. In May 1937 her physician incised a gland on the right side, obtaining little pus, and gave the patient another dose of roentgen radiation to the area incised. The condition did not improve after this, and the patient came to the University Hospital for advice.

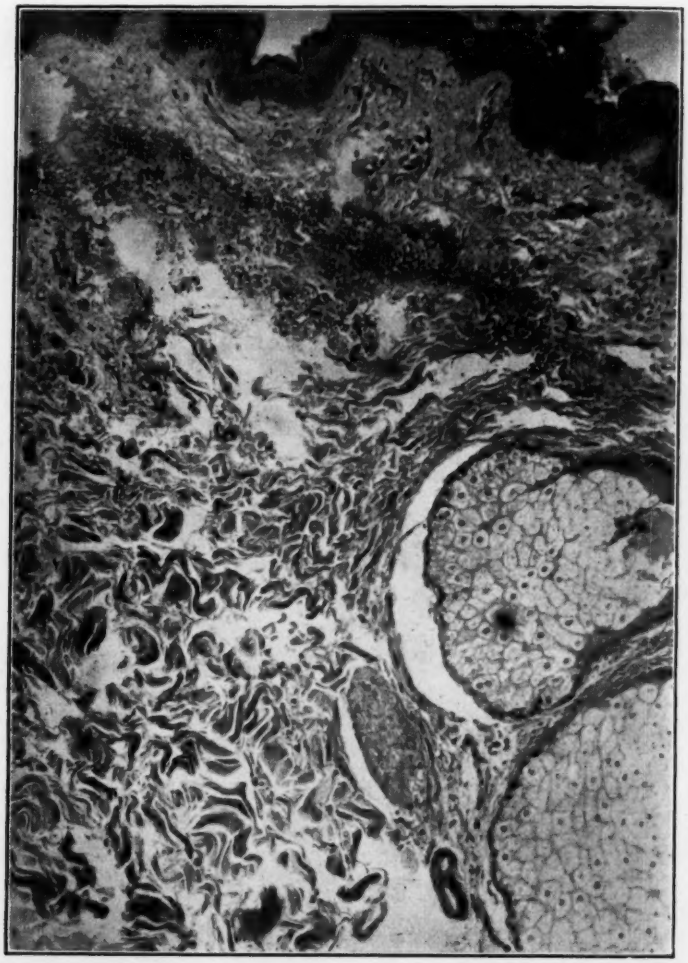
At the time of admission there were no symptoms referable to the skin, with the possible exception of inability to open the mouth widely, which she attributed to the swollen glands. She had had a moist cough for about a month prior to her visit here but had raised no sputum. She gave no history of malaise, night sweats, elevation of temperature or cutaneous eruption. She had had measles at 11 years and tonsillitis at 13 and had undergone tonsillectomy in 1935. She had been in good health, otherwise, all her life. Her catamenia had begun at 13 and had always been regular and of normal amount. Her parents and six living siblings were in good health. One sister had died of pulmonary tuberculosis at 15, when the patient was 5 years old.

Examination revealed a normally developed and nourished healthy-looking adolescent girl who looked a little dull and apathetic but was responsive and cooperative. The temperature was 98.4 F., the pulse rate 68 per minute and the respirations 18 per minute. Examination revealed no abnormalities aside from the remarkable change in the skin and in the neck. There was an obvious increase in the soft tissue of the neck, particularly on the right side, where there was a sinal mouth from which a small amount of thin seropurulent exudate could be expressed. The increase in the mass of soft tissue appeared on palpation to be made up of enlarged, matted lymph nodes.

---

14. Buschke, A., and Ollendorff, H.: Sklerödema adultorum mit muskulärer Lokalisation, Med. Klin. **37**:1406 (Sept.) 1927.

The sclerotic involvement was not universal. It was most marked in the nuchal region; from there it extended upward into the scalp and forward onto the face, where it spared only the eyelids, the nose and the lips; it was particularly noteworthy that not the slightest wrinkling of the forehead occurred when the gaze was forced upward. Involvement extended over the anterior portion of the



Photomicrograph of section of skin of the right side of the neck, stained with hematoxylin and eosin (approximately × 78).

neck and downward over the chest, where it spared only the nipples and the mammary areolas; it extended over the back, where it faded out gradually along the costal margins anteriorly and just above the buttocks posteriorly. The arms, the forearms and the hands were involved, only the fingers and the palms being spared.

The cutaneous change was observed to consist chiefly of remarkable resistance to pressure; the student who first examined the patient described the skin as

"boardlike," and subsequent examinations confirmed this impression. The skin was smooth, moderately pale and stiff; the subcutaneous tissue, instead of being loose and pliable, was firm and resisted all efforts to change its configuration. It was increased in amount. Normal wrinkles, furrows and bony landmarks were obliterated; the skin could not be picked up in folds, and normal movements of the body, such as lateral rotation and forward flexion of the head, were markedly limited. Mild acne vulgaris was noted in the usual sites of election for this disease. Physical examination revealed no other abnormalities.

Laboratory Examinations.—Urinalysis showed no albumin (by heat and acetic test) or sugar (by Benedict's reagent). Examination of the blood showed 75 per cent hemoglobin (by Sahli's method), 4,500,000 red cells and 4,800 white cells per cubic millimeter; the differential count showed 68 per cent polymorphonuclear neutrophils, 31 per cent lymphocytes and 1 per cent eosinophils; there appeared to be a normal number of platelets. A roentgenogram of the chest in postero-anterior stereoscopic projection showed no evidence of pulmonary disease. The Kahn reaction was negative. A stained smear of the exudate obtained from the sinal mouth showed no acid-fast bacilli, and cultures of this material showed no growth after three months. The basal metabolic rate was —18 per cent on Aug. 5, 1937, and —11 per cent on August 9. On August 20 there were 8.5 Gm. of serum proteins per hundred cubic centimeters, of which 3.1 Gm. were albumin and 5.4 Gm. globulin, the albumin-globulin ratio being approximately 0.6. The cholesterol content of the blood was 176 mg. per hundred cubic centimeters. On September 22, after the patient had been receiving desiccated thyroid gland in a dose of ¼ grain (0.016 Gm.) twice a day for six weeks, the basal metabolic rate was —14 per cent, and the serum proteins had risen to 7.8 Gm. per hundred cubic centimeters, the albumin-globulin ratio at this time being 1.

Histologic Picture.—A biopsy specimen taken from the immediate region of the sinal mouth was reported as showing "active chronic tuberculosis, a necrosing surface, with some vascular pyogenic granulation tissue, and no neoplasm." Examination of portions of the skin at a little distance from the sinal mouth revealed changes which while moderate were remarkable. The epidermis and the subpapillary portion of the corium were unaltered in appearance except for a small amount of round cell infiltration. The deeper layers of the corium showed marked enlargement of the bundles of collagen and separation of these from one another. No special stains were used, as only formaldehyde-alcohol fixation was done.

The patient's skin improved gradually from the time of her original examination here, so that late in September, nearly three months after she was first seen, involvement had receded to the level of the midforearms, the breasts and the inferior angles of the scapulas. The face, however, was still definitely involved at the time of discharge, on Oct. 15, 1937, as evidenced by failure of the forehead to wrinkle when the patient gazed upward.

COMMENT

It is felt that the finding of tuberculous cervical lymphadenitis in this case deserves comment. I am inclined to regard it as an incidental rather than an etiologic factor, for two reasons: 1. No such finding has been described in any previously reported case of this disease. 2. Several cases have been reported in which no infection of any sort preceded or accompanied the cutaneous changes. The reversal of the

normal ratio of serum albumin to serum globulin and the subsequent return of the ratio to normal are of interest. Similar observations were reported by Buschke.

SUMMARY

The history, the clinical and histologic characteristics and the differential diagnosis of scleredema adultorum (Buschke) have been briefly discussed. A case of this little recognized syndrome, unusual in that the backs of the hands were involved and in that the condition was associated with tuberculosis of the cervical lymph nodes, is described.

Prof. Udo J. Wile permitted me to report this case and made valuable suggestions.

CLINICAL APPLICATION OF A STAIN FOR SPIROCHETES (KRAJIAN)

STANLEY O. CHAMBERS, M.D.
AND
JULIUS R. SCHOLTZ, M.D.
LOS ANGELES

The diagnosis of syphilis in the seronegative stage, with its great importance to the patient, is dependent entirely on finding the causative organism in the primary lesion. At present the dark field method is the only one in general use, but most interested workers in the field admit that its use is not widespread enough. Stokes [1] stated: "Identification of the Spirocheta pallida in secretions and tissues has sustained a *regrettable delay in popularization* in part through the intrinsic difficulty and inconvenience of the methods which we are obliged to employ." In order to determine if possible how many average practitioners employed the dark field in diagnosis of early syphilis, several years ago one of us (S. O. C.) sent a questionnaire to one hundred physicians, with the following interesting result:

Performed own dark field	2%
Sent patient to laboratory	40%
Waited for serologic reaction to become positive	58%

Although this is a small series, nevertheless it should give a fair indication of the practice in a metropolitan center. It is not unreasonable to expect that in rural communities closer to 90 per cent of patients are allowed to reach the seropositive stage before treatment is begun.

REASONS FOR INFREQUENT USE OF DARK FIELD

There is no doubt that the dark field procedure presents formidable objections, both practical and theoretical. The following are the main reasons for the hesitancy of the average practitioner in the application of the dark field method: (1) the need for special equipment, (2) the need for special training in identifying the organism, (3) the difficulty of obtaining a proper specimen of serum, (4) the patient's objection to

---

Read before the Section on Dermatology and Syphilis, California State Medical Association, Del Monte, Calif., May 3, 1937.

From the Department of Medicine (Dermatology and Syphilis) of the Medical School of the University of Southern California and the Syphilis Clinic of the Los Angeles County Hospital.

1. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934.

going to a public diagnostic laboratory, (5) the time required for thorough dark field study and the necessary repetitions of the examination, (6) the small chances of success with old and locally treated lesions and (7) the lack of dark field apparatus and a diagnostic laboratory in many small communities. We believe that the method to be described eliminates many of these objections and at the same time offers a highly efficient method of demonstrating Spirochaeta pallida in syphilitic tissue.

METHOD

For the past five years in the department of syphilis of the Los Angeles County Hospital we have made clinical use of a staining method [2] (developed by A. A. Krajian of the department of pathology) for the identification of S. pallida in lesions suspected of being syphilitic. We have used it in nearly 500 cases, the material including tissue from subjects with all types of cutaneous and visceral syphilis, as well as autopsy material. The present communication will deal only with its use in cases of primary syphilis. The following is a brief comment on the stain by Krajian [3]: "Continued experience with this procedure has served to confirm its advantages over the original staining methods. In brief, the advantages are (*a*) rapidity and ease of performance and (*b*) reliability of result. The time required for the entire procedure is considerably less than one hour and gives the clinician at least a fairly rapid diagnosis. The simplicity of the method is attested by the fact that student technicians have had no difficulty in producing well stained preparations at the first attempt. The reliability of the method has been adequately checked both clinically and serologically and controlled by using tissue known to contain Spirochaeta pallida (fetal syphilitic liver). Confusion of nerve fibers and elastic tissue fibers with spirochetes has undoubtedly been a source of error in the past, but this is prevented by preliminary treatment of the tissue with a uranium salt."

Part to Be Played by the Physician.—The procedure is essentially the removal of a small piece of tissue from the suspected lesion, placing it in solution of formaldehyde and sending it to a laboratory for staining. The staining procedure requires less than an hour. The tissue is sectioned by the rapid frozen technic.

Biopsy would appear to be a rather heroic and unnecessarily complicated procedure, and yet we believe that in the average case it is actually less so than is the properly done dark field examination, which in many instances requires considerable manipulation and trauma of the lesion and often great discomfort to the patient.

A solution of from 2 to 4 per cent of procaine hydrochloride or butyn is used on the edge of the lesion, and a piece of tissue 2 by 5 mm. is removed with scalpel, manicure scissors or biopsy punch. The tissue is placed in 10 per cent solution of formaldehyde and sent to the laboratory.

---

2. Krajian, A. A.: (*a*) Modification of Dieterle's Method for Demonstrating Spirocheta Pallida in Single Microscopic Sections, Am. J. Syph. **17**:127-129 (Jan.) 1933; (*b*) Rapid Method of Staining Spirocheta Pallida in Single Sections of Tissue, Arch. Dermat. & Syph. **32**:764-767 (Nov.) 1935.

3. Krajian, A. A.: Personal communication to the authors.

PRACTICAL ADVANTAGES

1. The entire procedure requires from five to ten minutes.

2. The apparatus is present in any office (no expensive equipment).

3. The patient is not traumatized to obtain serum from the depths of a lesion.

4. He is not required to go to a laboratory.

5. The method is more accurate and practical for the rural physician than is the use of a capillary tube and indirect dark field examination.

GENERAL AND TECHNICAL ADVANTAGES

1. The stained slide can be kept as a permanent record. (The stain seems stable, as slides several years old remain distinct.)

2. Old and treated lesions show a high percentage of positive results (because tissue below the surface can be examined).

3. Saprophytic confusion forms are no problem, because they are surface organisms. This subject will be discussed later.

4. The method can be used for lesions of the mouth, again because confusion forms are not present. This subject will be taken up later.

5. The laboratory of the local health department can play an important part in detecting the disease in rural communities.

IDENTIFICATION OF S. PALLIDA

The problem of identifying S. pallida in the dark field is not a great one under ideal conditions, but unfortunately these do not frequently prevail. Because of the common location of primary syphilitic lesions, saprophytic spiral organisms must be taken into consideration. Many students of the spirochetes, including Hoffman [4] and Noguchi [5] have stated that they are unable to identify S. pallida definitely in the presence of other organisms, and therefore will not make a diagnosis on dark field examination unless the fluid to be examined contains one type of organism only.

Furthermore, in a recent publication by Mahoney and Bryant [6] it has been shown that the dark field examination of material from the mouth is unreliable because of the presence of organisms in the normal mouth which are indistinguishable from S. pallida.

Since all the saprophytic organisms are surface inhabitants, with the possible exception of Vincent's spirillum, it seems obvious that biopsy

---

4. Hoffman, E.: Personal communication to the authors.

5. Noguchi, H.; Jordan, E. O., and Falk, I. S.: The Newer Knowledge of Bacteriology and Immunology, Chicago, University of Chicago Press, 1928, chap. 36.

6. Mahoney, J. F., and Bryant, K. K.: Darkfield Diagnosis of Tonsil Lesions, Ven. Dis. Inform. **15**:385-386 (Dec.) 1934.

completely avoids the problem of the confusion form. Furthermore, it was stated by Stitt [7] and Noguchi [8] that S. pallida is the only organism that retains its morphologic characteristics after death. Therefore, the finding of a morphologically characteristic spiral organism within the tissue makes the diagnosis much simpler, since, in the northern hemisphere at least, other pathologic conditions caused by spirochetes in the tissue are rare.

Although it is true that the saprophytic confusion form is eliminated, we must issue a warning that certain artefacts in the stained tissue may

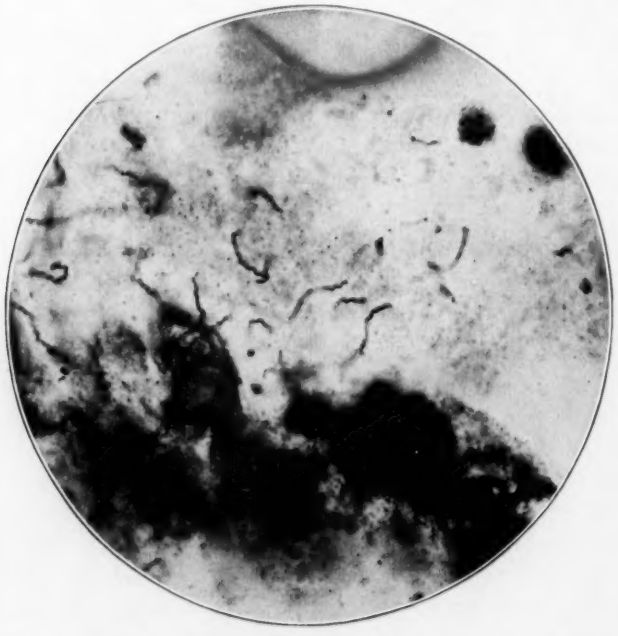


Fig. 1.—Liver of a congenitally syphilitic subject (recent stain), × 1,150.

roughly resemble S. pallida and that therefore the same rigid morphologic criteria must be applied and insisted on when a diagnostic examination of the slide is made as when the dark field procedure is employed. The organism when stained in the tissue shows its same sharp spirals closely set. It is unusual for the entire length of the organism to be apparent in one plane, but if one focuses with the fine adjustment of the microscope through several planes of the section, the organism will be revealed in its entire length. The accompanying photomicrographs (figs. 1 to 5) give an accurate conception of the appearance of the organisms stained in the tissues.

7. Stitt, E. R.: Practical Bacteriology, Blood Work and Parasitology, ed. 8, Philadelphia, P. Blakiston's Son & Co., 1927.

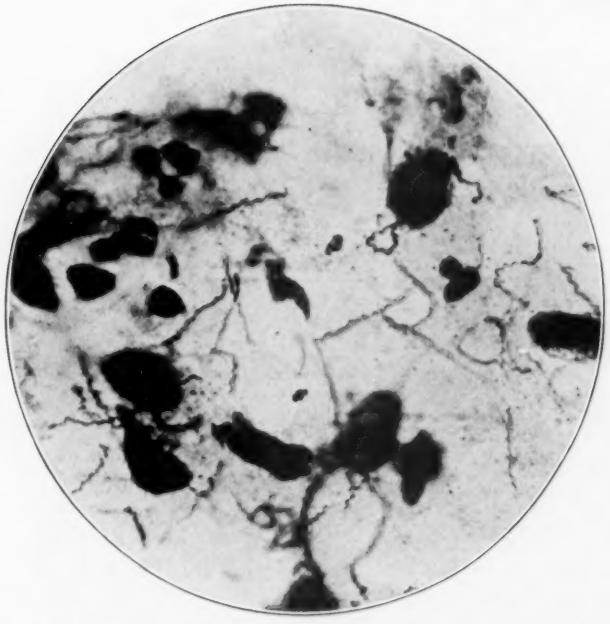


Fig. 2.—Penile ulcer of six weeks' duration. The Kolmer and the Kahn reaction were strongly positive in this case. The Krajian stain gave positive results.

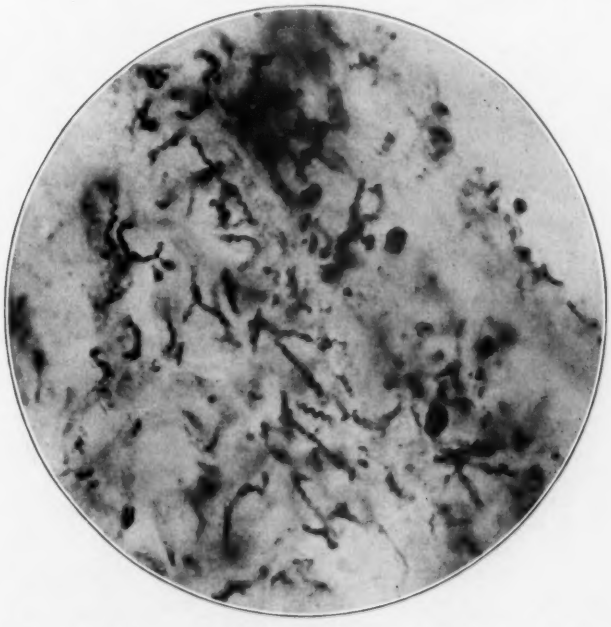


Fig. 3.—Penile nodule of two and one-half months' duration which had ulcerated several weeks before this photograph was made. Serologic tests had given negative results repeatedly. The Krajian stain gave positive results. The lesion healed in ten days, and the Kolmer and the Kahn reaction became 4 plus on the fourteenth day of treatment ($\times$ 1,150).

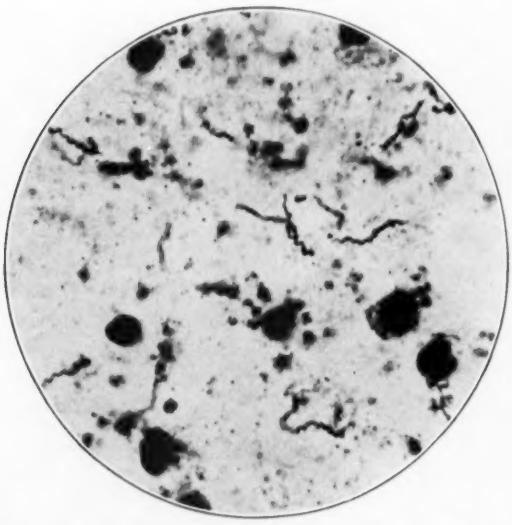


Fig. 4.—Maculopapular syphilid from a patient whose serologic reactions were strongly positive. The Krajian stain gave positive results. The section is from a labial mucous patch (× 1,150).

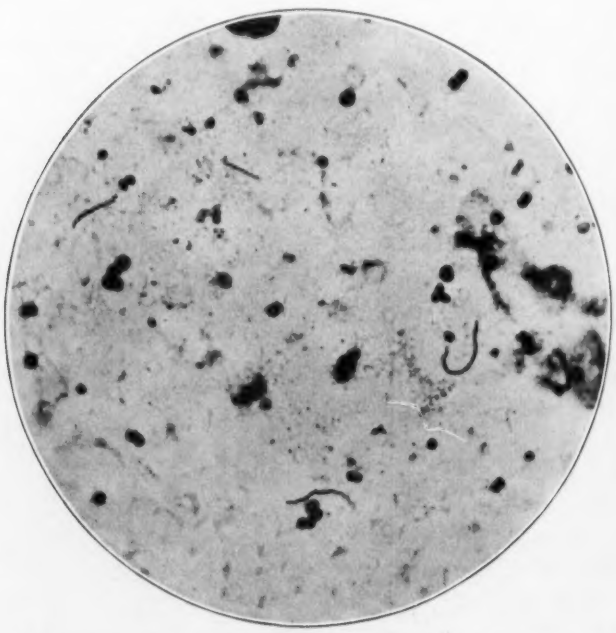


Fig. 5.—Congenital syphilis in a 12 day old infant with "snuffles." The material stained is taken from a smear of nasal discharge (× 1,150).

RESULTS IN SUSPECTED PRIMARY LESIONS

In a group of one hundred and four lesions suspected of being chancres the following results were obtained (these represent the average run of lesions in cases observed in the clinics and wards of a large general hospital):

Total examined	104
Proved syphilitic	86
Dark field examination and stain positive	46
Dark field examination negative; stain positive (dark field examination not done in 6)	39
Dark field examination positive; stain negative	1

From these figures it may be seen that the stain for spirochetes gave positive results in 98.8 per cent of cases, while the dark field procedure gave positive results in 55 per cent. Thus, the stain adds 43 per cent efficiency in isolating the spirochete in suspected lesions. The obvious criticism of our figures is that the stain appears to be highly efficient only because our dark field technic was poor. However, in a large group of primary lesions in all stages (as were ours) Stokes [1] found the average positive efficiency to be 66 per cent. This was explained by the fact that, although the efficiency was 90 per cent or better in the first week, it rapidly dropped to 50 per cent in the fifth and sixth week and to 30 per cent in the eighth week. If, then, 66 per cent is a good average in a clinic with well trained personnel, ours must represent an average at least as good as that found among the general practitioners or in the average commercial laboratory.

VALUE IN PUBLIC HEALTH PROGRAM

We should like to emphasize our belief that this method can be employed in the general program against syphilis. It is too much to expect the average physician and laboratory technician to become suddenly expert in the identification of S. pallida in the dark field preparation. It would be possible, however, for the health department of each county to have a technician to do the staining and a pathologist to examine the slide. The tissue could be mailed or delivered from any point in the county or the state within twenty-four hours and the report sent by telegraph or telephone if positive. This, incidentally, would give the health department an exceedingly accurate measure of the number of cases of infectious disease.

The biopsy in solution of formaldehyde has several advantages over the capillary tube method: The preparation is not fragile. There is no limitation of time. The temperature is not important. The procedure is less expensive. A bottle of solution of formaldehyde is more ubiquitous than a capillary tube.

OTHER USES FOR THE STAIN

We have found this stain exceedingly helpful in many other cases besides those involving suspected primary lesions. It has shown spirochetes in many different types of secondary eruptions, in a small number of late cutaneous syphilids, in autopsy material and surgical specimens. We hope in the near future to report on these other uses.

CONCLUSIONS

1. In our experience the clinical use of a stain for spirochetes (Krajian) has been found accurate in identifying S. pallida in cases of suspected primary syphilis.

2. It has certain advantages which suggest a wider applicability than the dark field procedure.

3. Its use in the public health campaign against syphilis is suggested.

727 West Seventh Street.
1930 Wilshire Boulevard.

CITRUS FRUIT DERMATOSES

HERMAN BEERMAN, M.D.
PHILADELPHIA

GEORGE H. FONDÉ, M.D.
NEW YORK
AND
J. LAMAR CALLAWAY, M.D.
DURHAM, N. C.

Since citrus fruits are becoming more and more an integral part of the everyday diet and so-called sensitivity to these fruits is developing into a common problem,[1] it is our purpose to correlate the pertinent literature on this subject. Allergy to the fruit is certainly not the only factor that is important in a given case, and we shall attempt to demonstrate that many of the so-called manifestations of allergy are found, when analyzed, to be pseudoallergic reactions due to contaminants, to dyestuffs or to some cause entirely unrelated to citrus fruits.

Cutaneous and other diseases have been ascribed to citrus fruits for a long time. Bazin [2] in 1862 described dermatitis of the face and

From the Department of Dermatology and Syphilology, School of Medicine, University of Pennsylvania, John H. Stokes, M.D., Director.

1. Various allergists have commented on the frequency with which various allergic phenomena, cutaneous or otherwise, are produced by citrus fruit. F. S. Smyth, K. M. Bain and M. Stallings (Infantile Eczema: A Study Based on One Hundred and Sixty Cases, J. A. M. A. **97**:1291 [Oct. 31] 1931) found that 12 per cent of 112 infants with eczema reacted positively to orange. A. H. Rowe (Clinical Allergy Due to Foods, Inhalants, Contactants, Fungi, Bacteria and Other Causes: Manifestations, Diagnosis and Treatment, Philadelphia, Lea & Febiger, 1937) noted that 14 per cent of 175 patients were sensitive to citrus fruit (orange 8 per cent, grapefruit 4 per cent and lemon 2 per cent). O. M. Schloss (A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**:341 [June] 1912) remarked that orange was one of the most common of offending foods. Similar views were expressed by J. G. Hopkins and B. Kesten (Specific Sensitivity in Eczema, Tr. Internat. Cong. Dermat. **8**:602, 1930) and by A. I. Fink and L. N. Gay (Critical Review of One Hundred and Seventy Cases of Urticaria and Angioneurotic Edema Followed for a Period of from Two to Ten Years, Bull. Johns Hopkins Hosp. **55**:280 [Oct.] 1934; abstracted, J. Allergy **5**:615 [Sept.] 1934). W. C. Alvarez and H. C. Hinshaw (Foods That Commonly Disagree with People, J. A. M. A. **104**:2053 [June 8] 1935), in analyzing 500 cases of sensitivity to foods, found that in 6 per cent there was a reaction of some sort to orange.

2. Bazin, A. P. E.: Leçons théoriques et cliniques sur les affections cutanées artificielles et sur la lèpre, les diathèses, le purpura, les difformités de la peau, etc. Redigées et publiées par le docteur Guérard, Paris, A. Delahaye, 1862.

upper extremities in orange peelers. In 1887 White,[3] of Boston, called attention to citrus fruit dermatitis and pointed out that it did not occur in southern California because marmalade was not made there. Thibierge[4] reported on cutaneous eruptions in orange peelers in 1903, and in the same year Barries and Courtois-Suffit[5] attributed dizziness, headache and cramps to citrus fruits. Kober and Hanson[6] in 1916 stated the belief that citrus fruit dermatitis was an occupational hazard. During recent years many reports have appeared on this subject.[7] We shall group the reactions reported into four general

3. White, J. C.: Dermatitis Venenata: An Account of the Action of External Irritants upon the Skin, Boston, Cupples & Hurd, 1887.

4. Thibierge, G.: Eruptions professionelles médicamenteuse et similées, Prat. dermat. **2**:426, 1903; cited by Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 4, pt. 1, p. 553.

5. Barres and Courtois-Suffit, M., cited by White, R. P.: The Dermatergoses, or Occupational Affections of the Skin: The Trade Processes, the Responsible Agents and Their Actions, ed. 4, London, H. K. Lewis & Co., Ltd., 1934.

6. Kober, G. M., and Hanson, W. C.: Diseases of Occupation, Philadelphia, P. Blakiston's Son & Co., 1916, p. 368.

7. (*a*) Murray, F. A.: Dermatitis Caused by Bitter Orange, Brit. M. J. **1**:739 (May 21) 1921. (*b*) Wolfram, S.: Citronenüberempfindlichkeit, Zentralbl. f. Haut- u. Geschlechtskr. **49**:416, 1934. (*c*) Brezina, B., cited by Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 4, pt. 1, p. 571. (*d*) Müller, R.: Fingerdermatitis durch Apfelsinenschalen, München. med. Wchnschr. **73**:864 (May 21) 1926. (*e*) Noll, R.: Citronenholzmehl-Ueberempfindlichkeit, Zentralbl. f. Haut- u. Geschlechtskr. **38**:437, 1931. (*f*) Shapiro, D. D.: Skin Diseases of Workers, Vrach. delo **13**:1240, 1930; cited by Bray, G. W.: Recent Advances in Allergy, Philadelphia, P. Blakiston's Son & Co, 1937. (*g*) O'Donovan, W. J., cited by Horner.[7p] (*h*) Fanburg, S. J., and Kaufman, J. G.: Eczema Due to Lemon Peel, J. A. M. A. **97**:3901 (Aug. 8) 1931. (*i*) Whitehead, W. D.: Fingernail and Toenail Changes Associated with Common Skin Diseases, Pennsylvania M. J. **40**:260 (Jan.) 1937. (*j*) Kesten, B. M., and Lyons, R.: Dermatitis Due to Contact with Orange Peel: Case Report with Successful Desensitization, J. Allergy **3**:552 (Sept.) 1932. (*k*) Urbach, E., and Wiethe, C.: Aetherische Oele als Ursache von allergischen Haut- und Schleimhauterkrankungen, München. med. Wchnschr. **78**:2030 (Nov. 27) 1931. (*l*) Urbach, E.: Citronendermatitis, Zentralbl. f. Haut- u. Geschlechtskr. **37**:787, 1931. (*m*) Sulzberger, M. B., in discussion on Traub, E. F.: Dermatitis in Fruit Handler, Arch. Dermat. & Syph. **34**:1054 (Dec.) 1936. (*n*) Loeb, J.: Apfelsinenschalenreaktion (3 Fälle), Zentralbl. f. Haut- u. Geschlechtksr. **41**:552, 1932. (*o*) Wise, F., and Wolf, J.: Dermatophytosis and Dermatophytids, Arch. Dermat. & Syph. **34**:1 (Jan.) 1936. (*p*) Horner, Sibyl G.: Dermatitis from Oranges and Lemons, Lancet **2**:961 (Oct. 31) 1931. (*q*) Mackay, K., and Ireland, I.: Investigation into the Fruit Industry, Health Bull., July-September, 1928, p. 481; abstracted, J. Indust. Hyg. **11**:164 (Sept.) 1929. (*r*) White, C.: Acneiform Eruptions of Face; Etiologic Importance of Specific Foods, J. A. M. A. **103**:1277 (Oct. 27) 1934. (*s*) Stroud, C. M.: Allergic Dermatitis, J. Allergy

(Footnote continued on next page)

classes for the sake of discussion: (1) the true allergic reactions; (2) the reactions due to mycotic or parasitic contaminants; (3) the reactions due to dyes or preservative contaminants and (4) the pseudo-allergic reactions.

TRUE ALLERGIC REACTIONS TO ORANGE

In determining the actual cause of a true allergic reaction to the pulp or peel of citrus fruit one must take cognizance of the fact that the substances are complex and that whatever reaction is observed may be due to one or a number of compounds. For example, Horner [7p] found that several distinct fractions are obtainable from the orange tree. Neroli oil (oil of orange flowers N. F.) is obtained from the flower, oil of petitgrain from the leaves and shoots and "orange oil" from the peel. Orange and lemon oil contain, according to this investigator, 90 per cent *d*-limonene. Lemon oil contains camphene and octylene. Sulzberger [7m] reported an instance of sensitivity to the carotene found in carrots and in oranges. Urbach and Wiethe [7k] presented experimental proof in five cases that volatile oils may act as allergens not only on the skin but on the nasal and the oral mucosa. Urbach [7l] observed, in addition, acute sensitization of the skin of a worker sorting lemons from the oil squirting from the fruit. Patch tests with lemon and with orange peel produced a marked bullous reaction after the dermatitis had subsided, and application of the peel to the nasal mucosa produced a severe attack of sneezing. Orange peel did not produce such an attack. On the other hand, Kesten and Lyons,[7j] while successful in desensitization of one patient by subcutaneous injection of the soluble substances extracted from the peel with alcohol and ether, maintained that the oil from the peel was a primary cutaneous irritant. Certain patients are sensitive only to the outer side of the peel (O'Donovan [7g]). Sensitivity to the various fractions of the fruit may be induced orally (by absorption along the gastrointestinal tract), by inhalation, by contact or by rectal administration.[7w] For example, Wolfram [7b] cited the case of a patient who reacted positively to patch tests with lemon peel and negatively to tests with orange peel and in whom the oral administra-

---

2:118 (Jan.) 1931. (*s'*) Schur, A.: Dermatitis Venenata: Report of Case Due to Osage Orange, Arch. Dermat. & Syph. **26**:312 (Aug.) 1932. (*t*) Avit-Scott, J.: Case of Orange Dermatitis, Brit. J. Dermat. **46**:378 (Aug.-Sept.) 1934. (*u*) Schreus, H. T., in discussion on Modlmayr: Palisander bzw. Cocoboloholz-Dermatitis, Zentralbl. f. Haut- u. Geschlechtskr. **36**:728, 1931. (*v*) Kämmerer, H.: Allergische Diathese und allergische Erkrankungen, Munich, J. F. Bergmann, 1926. (*w*) Rowe, A. H.: Clinical Allergy Due to Foods, Inhalants, Contactants, Fungi, Bacteria and Other Causes: Manifestations, Diagnosis and Treatment, Philadelphia, Lea & Febiger, 1937. (*x*) Schloss, O. M.: A Case of Allergy to Common Foods, Am. J. Dis. Child. **3**:341 (June) 1912

tion of lemon juice caused the relapse of the dermatitis. Similar experiences were noted by Wise and Wolf [7o] in two patients in whom the ingestion of orange juice evoked a vesicular eruption resembling sago grains on the palms and the fingers. Manual contact with oranges, ringworm infection with monilia and "eczema" could be ruled out. The eruption resembled a trichophytid. The avoidance of orange juice cured a dermatitis of seven years' standing in Avit-Scott's [7t] case. The dermatitis could be reproduced by feeding the patient orange juice which she had prepared herself. If the juice were prepared by others and she only drank it, she felt only a prickling sensation. If, however, the juice trickled down over her chin or onto her hands dermatitis developed (see our case 2). Rowe [7w] cited a case in which allergic phenomena were induced in a certain patient if she went into a room where certain citrus fruits were on display.

The clinical features of true allergic dermatitis due to the various constituents of citrus fruit are practically identical with those of any contact dermatitis. White [3] and Bazin [2] found that the dermatitis was usually restricted to the hands, especially the left hand, in which the orange is usually held [7a] while being sliced. The essential oil gets smeared on the face by contact with the hands. The condition begins with smarting, which is quickly followed by general redness, swelling and edema of the skin. Tiny vesicles appear, exude and form crusts. Whitehead [7l] noted pitting of the finger nails due to sensitivity to orange peel. Occasionally a seasonal variation may be noted.[7d] This may be occasioned, as in Stroud's [7s] case of summer remission of dermatitis due to citrus fruits and nuts, by the fact that the patient does not eat the offending substances at a certain season.

In addition to contact dermatitis, citrus fruits may cause other phenomena on the skin and mucous membranes such as urticaria, aphthous ulcers, angioneurotic edema and gastrointestinal disturbances,[8] localized sweating and flushing of the head,[9] papulo-urticarial eruption from lemonade [7l] and the familiar carotenemia.

Usually a specific allergy to individual fruits exists, but there are times when patients are allergic to all citrus fruits or to pears and the pit fruits, a fact to which Vaughan [10] has called attention (group allergy). Allergy to fruits frequently exists without cutaneous reac-

8. Hollander, E.: Mucous Colitis Due to Food Allergy, with Report of Five Cases, Am. J. M. Sc. **174**:495 (Oct.) 1927. Rowe.[7w]

9. Karrenberg, C. L.: Beiträge zur Aetiologie, Symptomatologie und Therapie der Allergosen: Ueber eine aussergewöhnliche Manifestation einer Allergie und über Wechsel des Typus einer Allergose, Dermat. Ztschr. **63**:169 (Feb.) 1932.

10. Vaughan, W. T.: Allergy and Applied Immunology, St. Louis, C. V. Mosby Company, 1931.

tions, and positive cutaneous reactions less frequently exist when there are no ascertainable symptoms or disturbances. Urbach, apropos of this observation, pointed out that in one case the skin of the face alone was sensitive to patch tests and failure to take account of this local sensitivity is a frequent cause of failure to get positive reactions in cases of definite occupational dermatitis. In addition, sensitivity may exist for ten days after withdrawal of the offending fruit, and patients who have potential allergy may have this excited by drinking large quantities of orange juice. White [11] has said that conditions such as soil, climate, rain and stage of growth greatly influence the toxicity of plants. This fact may explain the cases of irritation by plants and fruits from one locality and the relative innocuity of plants and fruits of the same species grown in another locality (Vaughan,[12] celery). In one case of suspected citrus fruit dermatitis it seemed that the peel of California oranges was violently irritating while for a short time after application it appeared that the peel of Florida oranges was harmless. (There was a delayed positive reaction.)

We have recently observed two cases which illustrate the chief clinical features of true allergic dermatitis due to the various fractions of the orange.

REPORT OF CASES

CASE 1.—*True Allergic Dermatitis Due to Orange Peel.*—C. C., a housewife aged 26, presented a patchy vesiculocrustaceous dermatitis of the dorsa of both hands. General examination showed no abnormality. There was no family or personal allergic background. The dermatitis of the hands began about one year before admission to the hospital and was characterized by exacerbations and remissions. Application of roentgen radiation, lotions and salves gave only temporary relief. In addition, treatment by various measures, including the administration of staphylococcus toxoid and of thyroid, the application of wet dressings of potassium permanganate, of ointment of coal tar, of ichthammol ointment and of Castellani's carbolfuchsin paint and an increase in the vitamin intake, was of no avail. As a last resort and as a result of vague suggestions from the history, patch tests were made with orange juice and orange peel. The patient yielded positive reactions only to tests with the peel. Avoidance of orange produced complete healing in one month.

CASE 2.—*True Allergic Dermatitis Due to Orange Juice.*—L. R., a stenographer aged 20, presented a vesicular dermatitis with considerable edema of the cheeks and the perioral region. Various therapeutic measures produced improvement in the

11. White, R. P.: The Dermatergoses, or Occupational Affections of the Skin: The Trade Processes, the Responsible Agents and Their Actions, ed. 4, London, H. K. Lewis & Co., Ltd., 1934.

12. Vaughan, W. T., in discussion on Sulzberger, M. B., and Simon, F. A.: Arsphenamine Hypersensitiveness in Guinea Pigs: Experiments Demonstrating (*A*) Regional Geographic Variability in Susceptibility to Sensitization, (*B*) Chemical Specificity of Hypersensitivity and (*C*) Variation in Sensitizing Proclivities (Sensitization Index) of Different Brands, J. Allergy **6**:39 and 55 (Nov.) 1934.

condition, but it promptly relapsed. The subsequent relapses were always associated with a localization on the chin. This localization suggested something which the patient ate, and after she was carefully questioned, orange juice was suspected. Patch tests with orange peel, orange juice, rouge, ointments and grapefruit were made. The orange juice yielded the only positive reaction. Avoidance of orange and of orange juice resulted in complete clearing.

MYCOTIC OR PARASITIC DERMATITIS FROM ORANGE

In 1925 Kingery and Thienes,[13] in investigating an epidemic of fruit dermatitis, cultured yeasts which produced a similar dermatitis when applied to the skin of animals and nonexposed workers. They concluded that at least certain forms of fruit dermatitis may be classed as dermatomycoses. Four years later Sutherland-Campbell [14] reported on paronychia and attempted to prove the etiologic factor in an epidemic among orange workers. This observer not only confirmed by his experience the observations of Kingery and Thienes but attempted to prove that the condition in these cases was a true yeast infection. As a result of Sutherland-Campbell's studies, he concluded:

1. Certain of the cull oranges are a source of fungous infection to man. 2. The skin of the orange is highly resistant to this fungus. 3. The pulp of the orange is readily infected by the fungus. As far as can be determined, only those orange workers whose fingers are frequently in contact with the pulp or juice of the orange acquire this fungous infection. 5. The "yeastlike organism" that I believe to be the etiologic factor in these cases is the spore form, or gonidia, of a fungus of the family *Mucoraceae*. 6. The species has not been determined.

It is conceivable that handling of infected oranges by other than orange workers may be a source of dermatitis occasionally. Ayres [15] raised the significant question of whether "any of the cases of urticaria or any of the toxic effects which have resulted from eating large quantities of oranges might have some connection with this organism, when introduced into the gastro-intestinal tract." He further remarked on "a type of papular urticaria that develops particularly in Mexican children who work in the orange groves, and who eat as many oranges as they want."

It might be pertinent to mention here that dermatophytids of the fingers may, in the presence of a positive reaction to a patch test with orange peel, be mistaken for true orange dermatitis. This will be discussed later.

---

13. Kingery, L. B., and Thienes, C. H.: Mycotic Paronchyia and Dermatitis: Hitherto Undescribed Condition Apparently Peculiar to Fruit Canners, Arch. Dermat. & Syph. **11**:186 (Feb.) 1925.

14. Sutherland-Campbell, H.: Paronychia: Attempt to Prove Etiologic Factor in Epidemic Among Orange Workers, Arch. Dermat. & Syph. **19**:233 (Feb.) 1929.

15. Ayers, S., Jr., in discussion on Sutherland-Campbell.[14]

DERMATITIS FROM DYES OR PRESERVATIVE CONTAMINANTS

Recently attempts to improve the appearance and the ripening and keeping qualities of oranges have led to the use of many substances which may act as cutaneous irritants. This phase of the problem has been splendidly covered by Traub and his associates.[16] According to these authors, the vogue of "painting the orange" is of less than three years' duration. Among the chemicals which have been used in recent years to ripen the fruit artificially and to preserve it for distant markets are: ethylene gas, kerosene, paraffin, soap, wax and sodium borate. The fruit is washed in various fungicidal solutions of secret composition, and insect sprays are used by some growers. Other ripeners used at times are hydrocyanic acid gas and gases from the exhaust of the automobile. According to Traub's report, the dyes most commonly used to add color to citrus fruits are "yellow OB" (orthotolueneazobetanaphthylamine) and "a combination of two dyes similar to sudan I and sudan II except that one is formed by coupling xylidine and amidoazoxylene on betanaphthol, and the other by coupling orthotoluidine on betanaphthol, both processes being carried out in alkaline solution." Yellow OB contains one of the same radicals occurring in amidoazotoluene hydrochloride, a leather dye, which Schwartz [17] found productive of dermatitis. The dye does not penetrate the peel or reach the pulp as shown by patch tests. It is not an essential irritant, and hypersensitivity develops only after constant and repeated exposure to the dye or in cases of individual idiosyncrasy. Clinically the dermatitis due to the dye seems to be practically identical with a dermatitis produced by one of the natural ingredients of the fruit.

PSEUDOALLERGIC REACTIONS IN CASES OF SUSPECTED CITRUS FRUIT DERMATITIS

Under this category we wish to place cases in which there was apparent sensitivity to citrus fruit but in which the eruption was shown to have another cause. Our cases 3 and 4, observed privately by one of us (H. B.), led us to reinvestigate the nonspecificity of results of patch tests with citrus fruit peel and to reaffirm the primary irritating qualities of oil from the peel, especially that of lemon, a fact which Keston and Lyons as well as Traub and his co-workers pointed out.

---

16. (*a*) Traub, E. F.; Gordon, R. E., and Van Dyke, L. S.: Dermatitis from Dyed and Otherwise Treated Citrus Fruits, J. A. M. A. **108**:872 (March 13) 1937. (*b*) Traub, E. F.: Dermatitis in Fruit Handler, Arch. Dermat. & Syph. **34**:1054 (Dec.) 1936.

17. Schwartz, L.: Skin Hazards in American Industry, Bulletin 229, United States Treasury Department, Public Health Service, September, 1936, pt. 2.

REPORT OF CASES

CASE 3.—Mrs. R. S., a laboratory technician aged 29, was first seen June 17, 1935, when she had dermatitis of the fourth and the fifth fingers of the right hand of four years' duration. A patch test with oil from orange peel produced a strongly positive reaction in three hours. The patient was able to drink orange juice with no ill effect. For a week the patient noted improvement after ceasing to squeeze oranges. However, the eruption recurred and remained as a lichenified dermatitis. Patch tests with Florida and California orange peel and grapefruit peel were made. In one and a half hours the patch of California peel had to be removed, and in twenty-four hours the reaction was strongly positive. There was no reaction to the peel of the Florida orange in twenty-four hours but a strongly positive one in forty-eight hours. From that time to the present there have been exacerbations and remissions totally unrelated to the handling of citrus fruit. A mild pedal dermatophytosis seemed to have little effect on the status of the dermatitis of the fingers.

CASE 4.—Mrs. M. C., a worker in the kitchen of an institution, aged 45, on Oct. 17, 1934, had a varicose ulcer on the left ankle, a mild pedal focus of dermatophytosis, pruritus vulvae and an acute recurrent dermatitis of the hands. The last process was of about four months' standing. The blood and the urine were normal. Soothing local treatment produced subsidence of the major part of her trouble in one week's hospitalization. Four months later there was a severe recurrence on the hands, with extensions to the arms and the legs. In the interim the patient had been engaged in preparing food and handling linen. Questioning revealed the fact that she thought she was sensitive to grapefruit. Patch tests were made with the oil from grapefruit peel, wool, dyed gloves, bismarck brown, uniforms, perfume, various flowers, neoarsphenamine, dog hair and stuffing from a sofa. All the reactions, except that to grapefruit, which was strongly positive, and those to bismarck brown and sofa stuffing, which were questionable, were negative. In spite of the avoidance of grapefruit and other citrus fruits and of contact with the sofa, and in spite of repeated positive reactions to tests with citrus fruits, the patient continued to have attacks of the dermatitis.

These patients led us to investigate the probable irritating properties of the "juice of the peel."[71] Accordingly, patch tests were performed on twenty-seven normal subjects (medical students and staff physicians) none of whom gave a history of sensitivity to citrus fruit but eight of whom had some personal or familial allergy. Patch tests were made on all with orange, lemon and grapefruit peel from commercial fruit. The results of these tests were all negative for orange and grapefruit, while five subjects gave moderately positive reactions to lemon peel.[18]

18. Dr. L. Schwartz, in commenting on the results of our patch tests, stated: "There is a great difference in patching with citrus fruit gathered directly from the tree and with citrus fruit obtained from stores. Before the citrus fruit finally reaches the consumer's market, it receives various treatments, among which is a wax finish on the surface of the peel. This wax finish is applied in one of three ways: It may be brushed on cold with brushes; it may be sprayed on hot with sprayers, or the fruit may be immersed in a bath of melted wax. The largest percentage of the citrus fruit on the market is waxed in the last manner. You can readily see that patch testing with waxed citrus peel will not allow the actual

(Footnote continued on next page)

Five of the controls were tested with oil from orange and grapefruit peel, and all gave negative reactions. In six of nine tested with the oil from lemon peel positive reactions developed. In four cases they were severe and in two cases moderately positive. In several of the cases the reaction was so intense that the patches had to be removed within a few hours of application.

It seems from these findings that the oil in the concentration used in these tests is relatively irritating. This experience confirms the results of Kesten and Lyons and of Traub and his associates. Whether the subjects in cases 3 and 4 were more susceptible than others to the oil as it exists in the peel, whether they furnish examples of false positive reactions to patch tests or whether they are really sensitive to the peel of the citrus fruits but had dermatitis from some entirely unrelated cause is open to conjecture. Even prolonged removal of the patients from contact with the fruit did not effect a cure. On the other hand, continued contact with the fruit appeared to have no detrimental effect on the cutaneous disease. From these considerations one must, even in the face of a positive cutaneous reaction, consider other causes for the process under observation. In this connection a correlation between the positive reaction and the history and course of the condition is necessary. Various factors, such as fluctuations in emotional, nervous and physiologic activity of the cutaneous area tested, affect the reactivity, and the accuracy of the physician's conclusions depends on the close relation of symptoms and course to exposure to and withdrawal of the substances incriminated by patch tests. On the other hand, Zündel [19] assumed that a positive reaction has definite sensitization as

---

peel to touch the skin, or if it does touch the skin, it will do so imperfectly. The thickness of the coat of wax on the peel will determine whether the peel will come in contact with the skin. When the peel is removed from the fruit for the purpose of patch testing, the wax coating may or may not have been cracked; the oil in the oil cells of the peel may or may not touch the skin, depending on whether the peel itself has been cracked. The number of days that the orange has been kept in storage will have some bearing on how dry the peel is and how much oil there is left in it. All these things have a marked bearing on the results of patch tests and may account for many of the negative results obtained by the authors from testing with orange and grapefruit peel.

"I believe, from the experiments which I made, that oil of lemon, oil of orange and oil of grapefruit will irritate by far the larger proportion of skins if allowed to remain on in the form of a patch test, because I believe that *d*-limonene, which is the chief constituent of these oils, will irritate most skins if left on in the form of a patch test.

"Another reason why the patch tests with lemon peel may have given the authors more positive results than the tests with orange peel is that lemons are seldom waxed."

19. Zündel, W.: Erfahrungen mit Hautfunktionsprüfungen an 2,000 Patienten, Arch. f. Dermat. u. Syph. **173**:435 (Jan. 27) 1936.

its basis. He agreed with Rostenberg and Sulzberger,[20] however, that whether such sensitization is the cause of the existing dermatitis depends on the history as well as the results of patch tests.

SUMMARY AND CONCLUSIONS

1. A study of the literature of citrus fruit dermatitis suggests that the etiologic problem is not simply one of uncovering examples of dermatitis produced by simple allergens but one of analyzing a causal complex.

2. Citrus fruit dermatitis may be grouped into four classes: the true allergies; the reactions (specific or allergic) due to mycotic or parasitic contaminants; the allergic reactions due to dyes or preservative contaminants, and the pseudo-allergic reactions.

3. The true allergic cutaneous reactions are due to a number of the ingredients of the fruit and clinically do not differ from contact dermatitis of other causation.

4. The reactions due to mycotic or parasitic contaminants are produced among workers handling infected fruit and are thought to be due to a specific yeastlike organism.

5. The dyes or preservative contaminants have been recently observed, and lately a complete analysis of these substances has appeared in the literature.

6. In two of our cases positive reactions to products of the citrus fruit apparently had no relation to the existing dermatosis. On the basis of these cases and the results of patch tests made on twenty-seven normal controls, we have designated the dermatitis in these cases, probable due to some other cause than citrus fruits, as a pseudoallergic reaction.

7. It has been shown that oil from lemon peel may be a primary cutaneous irritant.

---

20. Rostenberg, A., Jr., and Sulzberger, M. B.: Some Results of Patch Tests: A Compilation and Discussion of Cutaneous Reactions to About Five Hundred Different Substances, as Elicited by Over Ten Thousand Tests in Approximately One Thousand Patients, Arch. Dermat. & Syph. **35**:433 (March) 1937.

SUBSURFACE MYCELIUM AND DYES

THEIR SIGNIFICANCE IN MYCOLOGIC STUDIES

JOHN W. WILLIAMS, M.D.
CAMBRIDGE, MASS.

The importance of study of subsurface growth has not been realized. Frequently the only site from which fruiting bodies can be recovered is the base of a surface mycelial colony. This suggests the possibility that mediums producing subsurface growth would yield more amply fruiting bodies.

Staining pathogenic fungi during growth has not been given adequate attention. The incorporation of acid dyes or of low concentrations of basic dyes [1] in mediums results in beautifully contrasted colonies and improves the clarity of the microscopic picture.

Miyake [2] found that 0.2, 0.5 and 1 per cent *Eosin bläulich* (*G*) could be incorporated in Sabouraud's proof medium and would serve well as a vital stain for the five pathogenic fungi he examined, without affecting their growth.

Previous studies [3] have shown that subsurface growths can be obtained by using amino acids or hydrolyzed hair or skin as the source of nitrogen, and dextrose as the source of carbon. If dyes are added to these mediums, the colony and its microscopic clarity are enhanced, and neither growth nor differentiation is sacrificed.

In general, there is greater ease in obtaining specimens for microscopic examination from subsurface than from surface growth. A small piece of medium containing the growth can be easily cut. By placing a cover glass on this bit of growth and pressing, so as to spread it, a picture comparable to in situ growth is obtained.

In this study the following mediums were used: *a*, eosin 0.25 per cent, d-glutamic acid 0.25 per cent, dextrose 4 per cent and agar 1.5 per cent; *b*, methyl blue 0.5 per cent, d-glutamic acid 0.25 per cent, dextrose 4 per cent and agar 1.5 per cent; *c*, eosin 0.25 per cent, peptone 1 per cent, dextrose 4 per cent and agar 1.5 per cent; *d*, methyl blue 0.5

1. Williams, J. W.: Proc. Soc. Exper. Biol. & Med. **31**:1173 and 1174, 1934; Williams, J. W., and Green, L.: ibid. **32**:625, 1934.

2. Miyake, I.: Jap. J. Dermat. & Urol. **25**:343, 1925.

3. Williams, J. W.: Science **83**:396, 1936; J. Lab. & Clin. Med. **22**:268, 1936; Am. J. Clin. Path. **6**:444, 1936; Urol. & Cutan. Rev. **41**:117 and 198, 1937; Arch. Dermat. & Syph. **36**:581 (Sept.) 1937; Am. J. M. Technol. **3**:153, 1937; J. Bact. **35**:305, 1938.

per cent, peptone 1 per cent, dextrose 4 per cent and agar 1.5 per cent; *e*, methyl violet 0.0005 per cent, peptone 1 per cent, dextrose 4 per cent and agar 1.5 per cent; *f*, methyl violet 0.0005 per cent, d-glutamic acid 0.25 per cent, dextrose 4 per cent and agar 1.5 per cent; *g*, methylene blue 0.001 per cent, peptone 1 per cent, dextrose 4 per cent and agar 1.5 per cent, and *h*, methylene blue 0.001 per cent, d-glutamic acid 0.25 per cent, dextrose 4 per cent and agar 1.5 per cent. All mediums were slanted and adjusted to p_H 5.6. The organisms were observed for two months. They grew at room temperature in diffused light.

Two saprophytic and twenty-five pathogenic fungi were studied with the following results:

RESULTS

The organisms studied took the stains selectively. Most of them took the acid stains (eosin and methyl blue) well. Possibly owing to their toxicity and high dilution and to the hydrogen ion concentration of the organisms the basic stains were not taken as well. In the following descriptions the mediums are designated by the letter used in a previous paragraph:

Achorion Schoenleinii.—On *b* the knurled, nodular mycelium took the stain well; on *c* the round and nodular spores and the amorphous masses took the stain well.

Candida Candida.—On *d* certain small and large spores and mycelia took the stain selectively and showed good differentiation. On *e*, *f*, *g* and *h* the organism showed sparse selective staining.

Endomyces Capsulatus.—On *a*, with the exception of a few large spores which did not take the stain, the spores were well stained. On *e*, *f*, *g* and *h* stained granules appeared in the growth.

Endomyces Dermatitidis.—On *a*, *b*, *c* and *d* the spores seemed to show little stain. On *e*, *f*, *g* and *h* the spores were faintly green.

Epidermophyton Inguinale.—On *a* certain amorphous masses, spores and nodular mycelia took the dye well. On *e* a rare blue spore was noted.

Epidermophyton Rubrum.—On *b* the largest yeastlike spores did not take the dye well.

Glenospora Gammeli.—On *a* a few spores were well stained. On *b* the growth was not stained well. On *c* certain spores and mycelia were well stained. On *f* a rare large spore was deep blue. On *e*, *f*, *g* and *h* the organisms showed a faint tint of bluish green.

Geotrichum Bachmann.—On *a* the mushroom-like mycelium took the stain best. On *c* both deeply stained and unstained spores were present. On *b* and *d* the spores and the mycelium took the stain irregularly. On *h* an occasional spore or mycelium took the blue.

Indiella Americana.—On *d* the large round spores were not well stained. On *e* deep blue stained and unstained spores were noted. On *g* the mycelial vacuoles were blue. On *h* the large spores were stained blue as on *h* and *f*.

Lichtheimia Sp.—On *a* certain mycelia took eosin well. On *e* blue was rarely noted in mycelium.

Microsporon Audouini.—On *a* certain spores, sacs and amorphous masses were well stained. On *b* and *d* all elements took blue well. On *c* the spirals and the sacs took the pink well. On *e* and *f* the amorphous masses and the vacuoles took the blue. On *g* the bulbous and the saccular mycelium showed a slight amount of dye.

Microsporon Gypseum.—On *a* fuseaux took the stain better than small spores, mycelium or bulbous mycelium; on *c* they took the stain selectively, and on *b* and *d* they did not take the stain. On *e, f, g* and *h* spirals, mycelium, fuseaux and spores seemed to take a slight amount of stain.

Scedosporium Apiospermum.—On *a* and *c* certain large double-contoured spores seemed to take the dye better than the small spores. On *b* and *d* certain of the large double-contoured spores were well stained, and on *e, f, g* and *h* certain of the large spores seemed to take blue, while the rest of the growth did not.

Monilia Albicans.—On *d* the dye brought out the double contour; the larger elements as a rule stained less deeply than the smaller ones.

Oospora Humi.—On *a* there was great selectivity on the part of spores and mycelium. Eosin was well taken. On *b* the dye was not well taken. On *d* there was marked selectivity, the larger spores not seeming to take the dye. On *h* only certain spores and hyphae took the stain.

Scopulariopsis Brevicaulis.—On *a, b, c* and *d* there was selectivity for spores and mycelium; on *b* giant mycelium seemed to take the dye best. On *e* an occasional area of mycelium took blue stain.

Sporotrichum Schenckii.—On *a* the large spores were stained brownish red; the staining of other elements was patchy. On *b, c* and *d* the smaller spores took the dye, while usually the larger ones did not; the staining of mycelium was patchy. On *e, f, g* and *h* an occasional large or small spore took the dye.

Trichophyton Balcaneum.—On *a* there was marked selectivity of staining for spores and mycelium; a few large spores did not take stain. Methyl blue did not stain well. On *e* a rare blue spore was noted.

Trichophyton Crateriforme.—On *a* some of the large giant sacs took the dye; certain amorphous masses were well stained. On *b* the nodular mycelium was deeply stained. On *e* the amorphous masses apparently took the dye. On *f, g* and *h* there were small bits of color in the growth elements.

Trichophyton Granulosum.—On *b* the bulbous hyphae sacs and sacs with amorphous masses and spores took blue stain.

Trichophyton Gypseum Asteroides.—On *b* the centers of growth seemed better stained than other elements. On *c* spores, spirals and spore bunches stood out. On *f* sacs and spore bunches did not seem to be stained.

Trichophyton Gypseum Lacticolor.—On *c* small and bat-shaped spores and portions of the mycelium seemed to take most of the dye. On *d* the larger spores seemed to take less dye.

Trichophyton Interdigitalis.—On *b* the bulbs and spirals seemed to take stain poorly.

Trichophyton Louisianicum.—On *a* the amorphous masses and certain spores and mycelia seemed to take deeper stain than other elements. On *e* certain spirals and vacuoles seemed to take the dye better. In general, the vacuoles seemed to take basic dyes.

Trichophyton Purpureum.—On *a* a few bulbs and hyphae took the dye better; sacs apparently with spores and round spores were well contrasted. On *b* there

was selective staining of the bulbous mycelium. The organismal pigment confused some observations.

Trichophyton Sulfureum.—On *a* a few small bulbs and areas of mycelium were better stained than the larger spores and bulbs. On *c* certain bulbs and spirals were better stained. On *e* many of the amorphous masses were deep blue. With the basic dye there was some staining of amorphous masses, bulbs and mycelium.

Willia Anomala.—On *c* there was good differentiation, certain nuclei and mycelia taking the stain well. On *e* certain nuclei took the dye. In general, basic dyes tended to stain certain nuclei.

It must be realized that the term stain is used broadly. These dyes are water soluble, and many would leave the cells if water was added. Stain is used interchangeably with concentration of dye.

"Pleomorphism" in the colony was not considered. It is hoped that study may allow me to recognize colonies regardless of this factor. The characteristics mentioned are therefore only the beginning of a tabulation.

COMMENT

It is not the purpose of this paper to describe microscopic observations. The organisms were studied to determine the value of subsurface growth and their selectivity for certain dyes. Therefore, no reference is made to investigators who have described microscopic appearances. It is assumed that those mentioned have already been described. This paper is written with the hope that others will study subsurface growth and the value of dyes in mediums.

The findings noted are only a sparse listing of those present. They appeared to be the most striking. They emphasize the variation in selectivity of organisms and organismal parts for dyes. It is probable that basic dyes would be attracted into acid areas of the growth and acid dyes into basic areas. Oxidation-reduction dyes in the oxidized states in cells may indicate death of the cell. Localization of dye may indicate metabolic activity, since metabolism varies with permeability and with hydrogen ion concentration. It is hoped that studies of single cells will give deeper insight into this problem.

Such studies as these may aid in answering the age-old question: Do fungi imperfecti have a sexual life? The amorphous masses noted suggest pollination. These masses may be stained differentially, and it should be possible to trace the elements thus stained in slide culture with a medium in which organisms grow naturally and beneath the surface. My preliminary observations suggest that a sequence of events of this nature may exist with reference to the amorphous masses in some organisms. On several observations an end of mycelium enlarged; there was a congealing of amorphous protoplasm proximally and a saclike bulging distally. Apparently pressure increases in this sac, which finally ruptures and liberates the amorphous mass—a sequence of events strikingly similar to that seen in the development and extrusion

of the mammalian ovary. The link to sexuality may be found by tracing elements of the amorphous mass into the intact spore. This spore in certain cases seems to develop by the sac method just described. Using a medium which produces subsurface mycelium and dyes for contrast seems a logical procedure in this problem.

An objection may be raised to the preceding assumptions since the pressure necessary in the preparation may have ruptured the large sacs. Another objection might be that the amorphous masses are degenerative material which either exudes from the wall of the spore or is released when this wall loses its integrity. Neither of these questions can be answered in the present paper. The observation of amorphous masses is not entirely new. Dr. Ethel Rockwood has photographed them but to my knowledge has not discussed them in print. They deserve further study.

The exact nature of the mycelium and spores varies in many instances with the medium and the dye used. Growth with eosin seems most like that in the control medium. The high concentration of methyl blue used is probably toxic and responsible for poor growth. Methyl violet, even in the small concentration used, is apparently toxic, and this toxicity is responsible for poor growth. Methylene blue in the concentration used seems to lack toxicity.

The mycelium and the spores using methylene blue are not in all instances comparable to those using eosin. The greater photodynamic effect of eosin may be important; in a few instances eosin seemed to encourage surface growth. The oxidation-reduction effects of methylene blue may be important, since the dye is known to catalyze these reactions under certain conditions. For these reasons, the growths are not entirely comparable. In a few instances the dilute methylene blue used, instead of exerting toxic basic properties, seemed to stimulate growth; this is in line with stimulatory properties of small amounts of toxic substances.

There is no evidence that the colorless spores and mycelium on methylene blue mediums do not contain methylene white. It is possible that a viable state maintains the dye in its reduced form.

Granules of dye are frequently noted in spores and mycelium. The coloration may be so slight that it is overlooked, especially when the growth possesses pigment of its own. The fact that methyl violet and methylene blue are especially liable to reduction suggests the possibility that slight color may be indicative of an almost completely reduced condition.

Slide preparations, as previously outlined, are more difficult to make from Sabouraud's proof medium. It is hoped that after further study

amino acids can be substituted for peptone in the medium. The attainment of typical subsurface growths and of increased dye selectivity should stimulate such study.

CONCLUSIONS AND SUMMARY

When dyes are incorporated in mediums, growths take the dye as they develop, and factors underlying the selectivity can be studied. When dyes are used, elements of growth can be visualized more easily both microscopically and macroscopically.

By subsurface growth many elements typical for the organism develop. This growth varies so that it may be used in differentiation.

There is an optimum concentration of dye for use in a medium, one which is not too toxic and which will color growths selectively.

Oxidation-reduction dyes, such as methylene blue, may prove valuable in indicating cellular viability. Work is in progress to determine whether the cells which take methylene blue stain are in an oxidized (dead?) state and those which remain uncolored possess reducing (living?) substances and methylene white.

Observations of the amorphous mass suggest further studies of fungi imperfecti with reference to sex by the methods outlined here. Since this mass may take water-soluble dyes, as may mycelium and spores, a possible protoplasmic constitution is suggested.

SQUAMOUS CELL EPITHELIOMA IN PSORIATIC PATCHES

HERMAN CHARACHE, M.D.
BROOKLYN

The development of epithelioma on areas of skin affected with psoriasis is extremely rare. In the small number of cases reported the condition was of the basal cell variety.[1] In a larger number of cases basal cell epithelioma was associated with but did not involve patches of psoriasis. Flint and Gordon [1f] reported a case in which basal cell epithelioma developed on the right shoulder in the midst of a patch of psoriasis and squamous cell epithelioma of the scalp. It was not stated whether the squamous cell epithelioma involved the area of the scalp affected by psoriasis.

The association of hyperglycemia with psoriasis was emphasized by Pick,[2] who found an almost constant increase in the sugar content of the blood in 15 cases he studied.

In the case herewith reported treatment was given for epithelioma of the shoulder arising from a psoriatic patch. A second psoriatic patch, which was noted at the time of admission, underwent malignant transformation two years and four months later. Histologically the lesion proved to be squamous cell epithelioma.

REPORT OF CASE

R. M., a white man aged 76, was admitted to the Brooklyn Cancer Institute on June 22, 1934, complaining of a "sore" on the left shoulder. He stated that he had had psoriatic patches on his chest and back since 1920. The diagnosis was established by Dr. Raymond Clark, under whose care he had been since 1926. (This statement was recently confirmed by Dr. Clark, who treated the patient for diabetes and hypertension.) Two years previous to admission a psoriatic patch on the left shoulder began to ulcerate; it grew progressively larger until it reached the size of a half dollar, with a deep excavation in the center. Persistence of the lesion was first attributed to diabetes.

From the Brooklyn Cancer Institute (Dr. Ira I. Kaplan, Director), Division of Cancer, Department of Hospitals of the city of New York.

1. (*a*) Hutchinson, Jonathan: Arch. Surg., London **9**:223, 1898. (*b*) White, J. C.: Am. J. M. Sc. **89**:163, 1885. (*c*) Whitfield, A.: Brit. J. Dermat. **18**:40, 1906. (*d*) Fordyce, J. A.: The Pathology of Malignant Epithelial Growths of the Skin, J. A. M. A. **55**:1624 (Nov. 5) 1910. (*e*) Gray, A. M. H.: Brit. J. Dermat. **24**:325, 1912. (*f*) Flint, E. R., and Gordon, J.: Brit. J. Surg. **16**:321, 1928.

2. Pick, W.: Dermat. Wchnschr. **72**:297, 1921.

Examination revealed a punched-out ulceration over the left supraclavicular region, measuring 7 by 5 cm., with a deep necrotic excavated base measuring 2 cm. There were numerous psoriatic patches on the back and the chest; some of the patches on the chest were beginning to break down, forming sharply demarcated dull red areas, covered in part with grayish yellow scales and keratotic, bead-like granules. These would fall off and leave a bright red, moist and occasionally bleeding surface. The psoriatic patches on the back were all of the usual clinical type, as established by the clinical director of the institute, Dr. William E. Howes, and the rest of the staff.

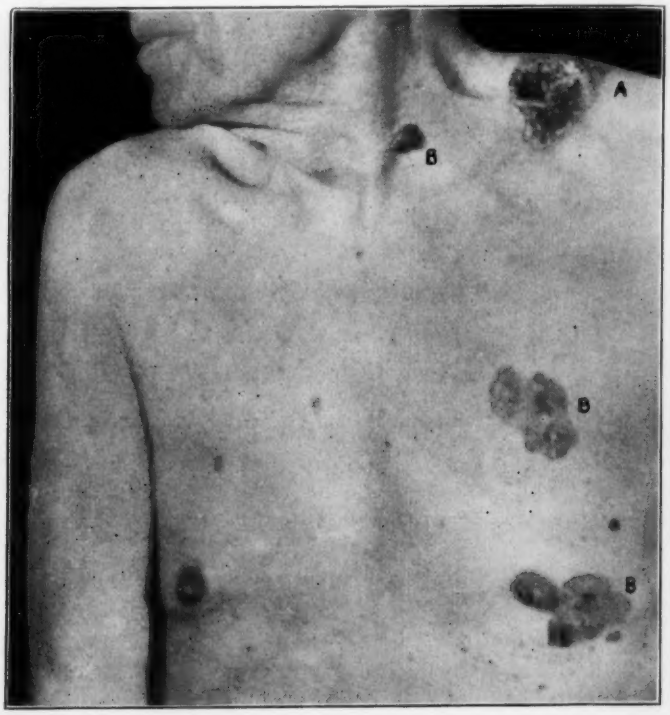


Fig. 1.—Photograph of patient, showing, *A*, squamous cell epithelioma of a psoriatic patch, and, *B*, psoriatic patches with keratotic granules.

The rest of the physical examination did not reveal any abnormality. The Wassermann reaction was negative. Chemical analysis of the blood showed 266.6 mg. of sugar, 22.7 mg. of urea nitrogen and 1.5 mg. of creatinine per hundred cubic centimeters. The urine showed 3 per cent sugar. The blood pressure was 230 systolic and 120 diastolic. A blood count was within normal limits. The temperature was normal, the pulse rate 80 and the respiratory rate 20. A biopsy specimen taken from the lesion was reported by Dr. S. H. Polayes, pathologist, to show "squamous cell carcinoma of the prickle cell type."

The patient received treatment by a wax mold containing 6 tubes of radon totaling 62 millicuries, and a dose of 3,000 millicurie hours was given over several days. The lesion healed completely.

On Sept. 23, 1935, the patient was readmitted to the hospital because of a lump on the left shoulder. Examination revealed a 3 cm. nodule close to the former healed lesion. This was excised and diganosed histologically as squamous cell epithelioma. The lesion was given a dose of 1,000 millicurie hours of radon by a wax mold containing 3 tubes of 17.6 millicuries. This lesion healed completely.

The patient was seen on Oct. 15, 1936, when he had an ulceration over a previously broken-down psoriatic patch on the left side of the chest close to the

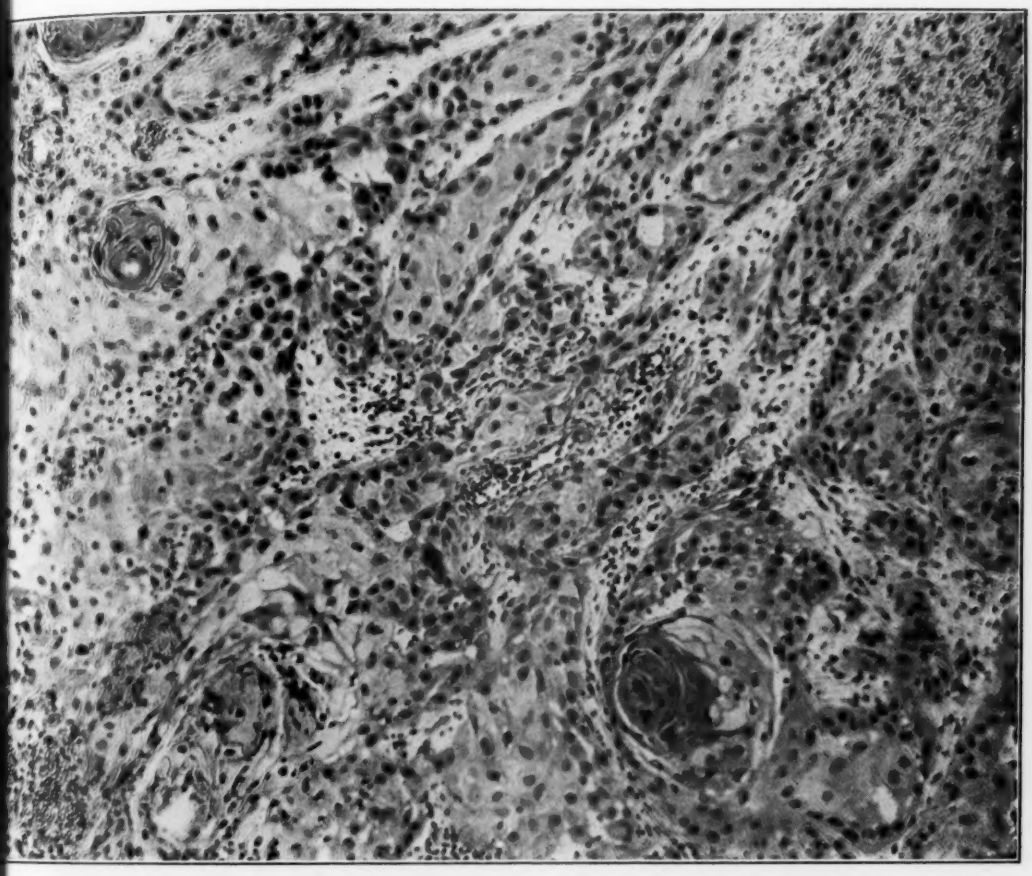


Fig. 2.—Photomicrograph, showing squamous cell epithelioma with pearl formation and numerous prickle cells (low power).

nipple. A biopsy specimen was taken from this lesion and reported as showing squamous cell epithelioma. At this time the patient complained of marked dyspnea and showed clinical evidence of pulmonary involvement. A roentgenogram of the chest showed effusion in the base of each lung. He refused to remain in the hospital and died at home on Nov. 26, 1936, from a condition clinically diagnosed as pulmonary metastasis.

SUMMARY AND CONCLUSION

The development of squamous cell epithelioma on psoriasis is rare. In the small number of reported cases the condition was of the basal cell variety, in most of them associated with but not involving the psoriatic patches. A case of squamous cell epithelioma involving psoriatic patches and associated with hyperglycemia is reported.

GRANULOMA INGUINALE

REPORT OF A CASE OF INVOLVEMENT OF THE UPPER LIP AND DEPIGMENTATION AND EDEMA OF THE VULVA

THOMAS B. HALL, M.D.
KANSAS CITY, MO.

It is now well recognized that granuloma inguinale is not limited to the tropics. Fox,[1] in reporting a number of cases in the middle part of the temperate zone, has called attention to the wide distribution of this disease. The present case is reported because of some unusual features.

REPORT OF CASE

M. S., an unmarried Negress aged 25, who was born and had lived all her life in Missouri, was first admitted to the Kansas City General Hospital on June 19, 1935. Her condition had started two years before as "bumps" around the vaginal opening, which gradually spread as running sores.

Although she stated that she had not had syphilis and serologic tests gave no evidence of the disease, she was given injections of neoarsphenamine and a bismuth preparation for several months. These had no effect on the ulceration.

There were no apparent abnormalities aside from the pudendal involvement. The labia majora and minora were completely involved by an extensive superficial granulomatous ulceration which freely exuded serosanguineous material. The inguinal glands were palpable but not enlarged or painful.

Histologic examination of the ulcerated edge of the lesion revealed a granulomatous structure with numerous plasma cells. No organisms were demonstrated in the tissue. The Wassermann and the Kahn test were negative.

A diagnosis of granuloma inguinale was made, and the patient was given intravenous injections of 10 cc. of a 1 per cent solution of antimony and potassium tartrate twice a week. Healing was complete at the end of nine months, and she was discharged April 9, 1936. At this time the extensive ulcerations of the labia majora and minora were completely covered with epithelium. Here and there were small scattered areas of depigmentation.

The patient was next seen on April 29, 1937, when she presented a sore on the upper lip and an ulceration around the external genitals. According to the history, the patient had cut her lip on a clothesline three months previously. One week later a sore appeared, which progressed to the extent shown in figure 1. A slight ulceration around the external genitals had been noticed six months after she left the hospital. Its progress had been slow but steady. About the same time she noticed that her private parts were turning white. This depigmentation had progressed to the stage shown in figure 2. She had lost 30 pounds (13.6 Kg.) during the last six months.

---

1. Fox, H.: Granuloma Inguinale: Its Occurrence in the United States, J. A. M. A. **87**:1785 (Nov. 27) 1926.

Examination of the pudenda showed that the labia majora and minora were fused and covered by epithelium which was completely depigmented except for a few pigmented islets here and there. The depigmented area was moderately edematous. Completely surrounding the depigmented zone was an area of ulcera-

Fig. 1.—Granuloma inguinale of the lip.

Fig. 2.—Granuloma inguinale of the genital region, showing depigmentation and edema of the labia, surrounded by ulceration.

tion of varying width extending from the mons veneris to the anus. This involved the vaginal orifice and approximately 1 inch (2.5 cm.) of the proximal portion of the vaginal canal. The ulcerated area exuded an abundant serosanguineous discharge. The inguinal glands were palpable but only slightly enlarged. The right half of the upper lip was involved by an extensive superficial ulceration with

an elevated margin. This ulceration completely covered one half of the vermilion border of the upper lip and extended about 0.5 cm. on the mucous membrane of the lip.

Laboratory Findings.—The Wassermann and the Kahn test were negative. Examination of the blood showed 4,100,000 erythrocytes and 50 per cent hemoglobin. The Frei test gave positive results. Histologic examination of the margin of the ulcerated area in the genital region showed marked acanthosis, with an underlying chronic granulomatous inflammatory infiltrate. Histologic examination of the margin of the ulcerated area of the lip showed changes which were essentially similar.

Course.—A diagnosis of granuloma inguinale of the lip and the perineum was made, and the patient was given 5 cc. of the fuadin intramuscularly twice a week. The first change noticed was a prompt abatement of the abundant secretion.

Healing of the ulcerated areas of the lip and the perineum was complete after fifty-six injections of 5 cc. of fuadin. Improvement in the general condition was prompt. The patient gained 30 pounds (13.6 Kg.) within two months after entering the hospital.

Though she was apparently cured, treatment with fuadin was followed by intravenous injections of 10 cc. of a 1 per cent solution of antimony and potassium tartrate twice a week for three months to prevent recurrence. Up to Jan. 28, 1938, she had shown no recurrence.

COMMENT

The depigmented edematous vulva surrounded by a zone of ulceration presented a bizarre and unusual appearance. The positive reaction to the Frei test was of possible significance in connection with the edema. However, careful questioning elicited no history of adenitis or of the anorectal syndrome of lymphogranuloma venereum.

Fox,[1] in an analysis of one hundred and fifty cases of granuloma inguinale in the United States, stated that "elephantiasic enlargement of the genitalia due to lymphatic obstruction and independent of filiariasis was observed in fourteen cases equally divided between the two sexes."

These cases were reported prior to the introduction of the Frei test. It would be interesting if in the cases in which granuloma inguinale was associated with elephantiasic involvement the Frei test could have been used. Could a latent coexisting infection with the virus of lymphogranuloma have played a role in the causation of this edema?

Involvement of the lip in granuloma inguinale, while not common, has been reported by Parounagian and Goodman.[2] The definite history of injury in my case, i.e., laceration preceding involvement of the lip, is interesting.

---

2. Parounagian, M. B., and Goodman, H.: Ulcerating Granuloma (Granuloma Inguinale): A Report of a Rare Example of This Disease in a Syphilitic Patient, Arch. Dermat. & Syph. **5**:597 (May) 1922.

Recently, Butts [3] attempted to incriminate the pubic louse as a vector of granuloma inguinale. Possibly the organism of granuloma inguinale is not able to penetrate the intact epidermis and the bites of pubic lice and the excoriations accompanying infestation produce a hiatus allowing the organism of granuloma inguinale to gain entrance to the skin.

902 Professional Building.

3. Butts, D. C. A.: Granuloma Inguinale: Preliminary Report on Certain Microscopic Observations, Am. J. Syph., Gonor. & Ven. Dis. **21**:544 (Sept.) 1937.

Clinical Notes

LXXXII.—PITYRIASIS VERSICOLOR INVOLVING THE INGUINAL REGION AND THE GENITO-CRURAL FOLDS

MORRIS MOORE, PH.D., ST. LOUIS

Mycologist to the Barnard Free Skin and Cancer Hospital, the Barnes Hospital and the Department of Dermatology, School of Medicine, Washington University

Inguinal or genitocrural pityriasis versicolor is so uncommon that the report of the following case is warranted:

REPORT OF CASE

M. P., a woman aged 35, entered the dermatologic clinic of the Barnard Free Skin and Cancer Hospital complaining of "spots" on her body which had per-

Pityriasis versicolor of the crural region and the thighs.

sisted for approximately five years. There was no complaint of pruritus or other subjective symptoms.

Examination revealed an extensive eruption of discrete and confluent chamois-colored macules involving the skin of the arms, the body, the thighs, the axillas and the genitocrural region. These lesions were not pronounced on the sternum but became more so as they spread to the lower part of the abdominal region,

---

Studies, observations and reports from the Laboratory for Mycology and Dermatological Research of the Barnard Free Skin and Cancer Hospital, service of Dr. M. F. Engman.

the breasts, the sides and the back. The heavily tanned arms showed by contrast light areas of similar outline to those of the body. Further examination of the crural region showed a confluent involvement of the labia majora, with the lesions becoming macular, punctiform, somewhat papular and furfuraceous as they spread to within a few inches of the knees on the inner aspects of the thighs.

Scrapings were made from various locations on the body, the arms, the crural region, the axillas and the thighs. In all material the organism, Malassezia furfur, to which this disease is attributed, was found in profuse numbers.

LICHEN RUBER MONILIFORMIS

Report of Observations at Necropsy

FRED WISE, M.D., AND CHARLES R. REIN, M.D., NEW YORK

Detailed reports of observations at necropsy of patients afflicted with dermatoses of unknown cause are only rarely published. We therefore take this opportunity to record the results of the postmortem examination in a case which we reported under the title "Lichen Ruber Moniliformis." [1]

After the publication of the report the patient had been seen on frequent occasions and at no time showed any change in the appearance of his eruption or in his usual general physical condition.

He was admitted to the Scranton State Hospital, Scranton, Pa., on March 5, 1937, in a state of coma. While sitting in a restaurant with his companions, he suddenly experienced severe precordial pain. He was apparently unable to cry out and struggled to rise from his chair. His companions stated that his arms shook as in a convulsion and he fell to the floor, striking his head against a radiator. He was taken to the dispensary, where he had three clonic convulsive seizures, the duration and extent of which were not recorded. No note was made as to the presence of fracture of the skull or other injury to the head. A roentgenogram of the skull on March 8, 1937, revealed no evidence of fracture. There were no signs of increased intracranial pressure.

General physical examination showed no abnormality except the eruption and bradycardia (the pulse rate being noted as 38). The ocular reflexes and the eyegrounds were recorded as normal. After he was admitted to the hospital, he had four or five convulsive seizures, starting on the right side of the body and spreading rapidly to involve the entire body, each attack lasting approximately three minutes. On the fourth day the patient presented signs of arterial occlusion in the left forearm, which was cold and white; the finger tips were blue. The brachial pulse could be felt only as far as the brachial bifiurcation. About three hours later a 5 inch (13 cm.) clot was removed, mostly from the ulnar artery. Despite this procedure, the arm became gangrenous and two days later was amputated. The patient never fully rallied from the operation and died the following morning.

Laboratory findings, including examination of the urine, the blood and the spinal fluid and a roentgenogram of the skull showed no abnormality except the presence of albumin and hyaline casts in the urine, a white blood cell count ranging from 10,000 to 18,000, with a slight increase in the polymorphonuclear leukocytes, and slight calcification of the pineal gland.

Necropsy, performed about two hours after death, indicated that the probable cause of death was cerebral hemorrhage.

While it was impossible for us personally to review the necropsy material, the microscopic sections of the brain, the lungs, the heart, the liver, the kidney, the pancreas and the spleen were placed at our disposal by Dr. Talcott Wainwright, of Scranton, Pa. They were studied carefully by Dr. Arthur Ginsler, in an attempt to correlate any visceral changes with the clinical and microscopic picture of the skin.

---

1. Wise, F., and Rein, C. R.: Lichen Ruber Moniliformis (Morbus Moniliformis Lichenoides), Arch. Dermat. & Syph. **34**:830-849 (Nov.) 1936.

RÉSUMÉ OF OBSERVATIONS AT NECROPSY

Lungs.—Three sections showed much passive congestion, with alternating areas of atelectasis and emphysema. There was a widespread patchy interstitial chronic inflammatory reaction, evidently a low grade pneumoconiotic process. This was in places nodular and consisted of an infiltration of lymphocytes, epithelioid cells, and foreign body giant cells. Much anthracotic pigment was present, some of it within phagocytes. A number of the arterioles showed moderate thickening.

Heart.—One section, including a coronary artery and a valve (apparently the left circumflex artery and the mitral valve), showed a few small foci of myocardial fibrosis but for the most part no significant change. The coronary artery showed mild atheromatous intimal thickening. Some of the arterioles within the myocardium were moderately thickened. No other vascular or parenchymatous damage was noted except a moderate vacuolar change of some of the auricular myocardial bundles at the base of the valve. The valve and the pericardium showed nothing of note.

Liver.—Two sections showed central passive congestion, evidently of short duration. There were a number of small focal areas of necrosis with polymorphonuclear leukocytic infiltration. Although two or three of these were as large as a low power field and approached the appearance of abscesses, they did not appear to be of bacterial origin but rather suggested a terminal toxic process.

There was occasional moderate arteriolar thickening. Much scattered pigment, possibly anthracotic, was present, some of it within the Kupffer cells.

Spleen.—One section showed passive congestion of the sinusoids, with atrophy of the follicles and possibly slight thickening of the cords. In places the pulp contained a number of polynuclear leukocytes and monocytes. Much pigment, probably anthracotic, was present. There were two small congenital cysts in the section. There was no evidence of vascular alteration.

Kidney.—Two sections showed a well preserved parenchyma with a few insignificant areas of fibrosis. There was mild thickening of some of the interlobular arteries and of a few arterioles. The glomeruli showed no change. Many of the collecting tubules showed granules of brownish pigment, whose nature was not certain, within their epithelial lining cells. Several small congenital cysts were present.

Pancreas.—Two sections showed no histologic changes of note.

Brain.—Several sections showed thrombophlebitis of the sagittal sinus and several of its tributaries, with a localized acute inflammatory reaction of the meninges in the vicinity. One section taken from the postrolandic area showed an area of hemorrhagic destruction the size of one and one-half low power fields. There was no definite perifocal reaction about this area, suggesting that it was either an artefact or a terminal incident.

The consensus was that there were no definite vascular or parenchymatous changes which could be correlated with the pathologic picture of the cutaneous lesions or which were not entirely consistent with the usual expected changes in any person of the patient's age. On the basis of this we are forced to conclude that the cutaneous eruption was not related to or associated with any morphologically demonstrable vascular or parenchymatous visceral lesion.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

LICHEN URTICATUS (PAPULAR URTICARIA): TREATMENT WITH PARATHYROID EXTRACT; THEORETICAL CONSIDERATION OF THE ETIOLOGY. DONALD M. PILLSBURY and THOMAS H. STERNBERG, Am. J. Dis. Child. **53**:1209 (May) 1937.

All dermatologists know, as Pillsbury and Sternberg point out, that the usual course of lichen urticatus is characterized by chronicity, frequent exacerbations and complete remission in the fall which lasts through the winter. The eruption has a striking seasonal incidence, occurring in some 85 per cent of cases from April to August inclusive.

The therapy originally suggested by Cornbleet consisted of oral administration of some calcium preparation (calcium lactate, calcium gluconate or dicalcium hydrogen phosphate) and subcutaneous injection of parathyroid extract at weekly or biweekly intervals, according to the severity of the process. The dose of parathyroid extract varied from 10 to 15 units per injection for infants and from 20 to 25 units for older children.

Good or excellent results were obtained in 85 per cent of 34 patients treated with parathyroid extract, topical applications and oral administration of calcium, as compared with 38 per cent in a group of 26 patients whose treatment did not include parathyroid extract. In many instances the itching was relieved almost immediately, and the papular lesions underwent involution in a few days.

(I have employed Cornbleet's method in 6 cases of typical lichen urticatus and can verify the prompt and striking response to this method of treatment.—Abstracter.)

EXTENSIVE XANTHOMA TUBEROSUM IN CHILDHOOD DUE TO INFECTIOUS CIRRHOSIS OF THE LIVER. FRED D. WEIDMAN and JOSEPH STOKES JR., Am. J. Dis. Child. **53**:1230 (May) 1937.

The case of a child with fatal jaundice and cutaneous xanthomatosis due to hypertrophic biliary cirrhosis is described. The authors did not believe that the condition was Christian-Schüller disease but felt that it belonged to the complex of xanthoma tuberosum, which occurs in adults in connection with hypertrophic cirrhosis of the liver. An exceedingly high cholesterol content of the blood (1,199 mg. per hundred cubic centimeters) was present. Another special feature was the development of xanthomatous changes in the scar of a wound following laparotomy and in the gums after extraction of teeth. The liver was examined histologically during life and showed cleancut hypertrophic biliary cirrhosis. Diabetes insipidus was present—in fact, it was the earleist clinical symptom.

NELSON PAUL ANDERSON, Los Angeles.

RACIAL INCIDENCE OF ACRODYNIA. J. ZAHORSKY, Arch. Pediat. **54**:56 (Jan.) 1937.

Zahorsky observed the interesting fact that of 60 children with acrodynia 51 were of German, 2 of Slovak, 1 of Polish, 2 of French, 1 of Irish and 3 of Scotch extraction. The ancestries of several patients were traced to southwestern Germany, where the disease is reported to be most prevalent.

ORR, Buffalo. [AM. J. DIS. CHILD.]

EXPERIMENTAL ARSPHENAMINE DERMATITIS: THE INFLUENCE OF VITAMIN C IN THE PRODUCTION OF ARSPHENAMINE SENSITIVENESS. F. E. CORMIA, Canad. M. A. J. **36**:392 (April) 1937.

From experimental studies Cormia found that variations in the vitamin C content of the diet in a group of guinea pigs had little if any influence on the development of cutaneous hypersensitivity to arsphenamine. A diet low in vitamin C predisposed toward more indolent and severe reactions. There was little inhibiting effect on the intensity or the frequency of the reaction from the second intracutaneous injection of arsphenamine (administered twenty-eight days after the first injection) when large doses of vitamin C were given. When a diet low in vitamin C was given to a group of guinea pigs which had been both sensitized and unsensitizable at different periods and to a group of guinea pigs which had never been sensitized, cutaneous reactions to arsphenamine were noted in approximately half the animals. Twenty-two guinea pigs were given large amounts of ascorbic acid, and these could not be sensitized to neoarsphenamine. Later, when these same animals were placed on a diet deficient in vitamin C, 7 reacted to injections of neoarsphenamine.

COOPERATIVE CLINICAL STUDIES IN THE TREATMENT OF SYPHILIS: THE EFFECT OF SPECIFIC THERAPY ON THE PROPHYLAXIS AND PROGRESS OF CARDIOVASCULAR SYPHILIS. H. N. COLE, L. J. USILTON, J. E. MOORE, P. A. O'LEARY, J. H. STOKES, U. J. WILE, T. PARRAN and J. MCMULLEN, J. A. M. A. **108**:1861 (May 29) 1937.

Among 6,253 syphilitic patients studied by the Cooperative Clinical Group who were treated for six months or longer, there were 9.9 per cent who manifested cardiovascular involvement at the time of admission or subsequently. It was found that 4.9 per cent had uncomplicated syphilitic aortitis, 4.1 per cent aortic regurgitation, 1.2 per cent aortitis with aneurysm and 0.8 per cent myocarditis. The percentage of Negro patients affected was three times that of white patients. In 43 per cent of the patients there was concomitant involvement of the central nervous system. It was noted that 69 per cent of the patients had had no treatment or only a little treatment with heavy metal prior to the detection of the cardiovascular involvement. While adequate early treatment is the best course, prolongation of life and symptomatic improvement followed therapy with heavy metals and potassium iodide by mouth. The arsenicals may be used cautiously in alternating courses with the heavy metals, provided preliminary treatment is well tolerated.

THYMOL THERAPY IN ACTINOMYCOSIS. H. B. MYERS, J. A. M. A. **108**:1875 (May 29) 1937.

Preliminary experiments by Myers showed that thymol possesses the power of destroying Actinomyces in forty-five seconds in 1:1,000 aqueous solution. Myers treated 5 patients with actinomycotic infection with thymol locally and systematically, and all recovered. Another patient who refused to take thymol internally died of visceral involvement. For local use Myers used a solution of from 10 to 20 per cent thymol in olive oil. For internal use thymol was administered by mouth in crystal form in capsules of 1 or 2 Gm. once daily or less frequently. It was given on an empty stomach. LEWIS, New York.

ARACHIDONIC AND LINOLIC ACID OF THE SERUM IN NORMAL AND ECZEMATOUS HUMAN SUBJECTS. W. R. BROWN and A. E. HANSEN, Proc. Soc. Exper. Biol. & Med. **36**:113 (March) 1937.

Linolic acid (tetrabromides calculated as such) is present in human serum to the extent of about 5 per cent of the total fatty acids, and arachidonic acid (polybromides calculated as such), in about 3 per cent of the total fatty acids in pooled

samples of the blood serum of normal children. The content of both these fatty acids is definitely diminished in children with eczema. In patients with active eczema which was clinically cured either by the internal administration of oils rich in the unsaturated fatty acids or by the local application of ointments containing crude coal tar or both, the arachidonic acid content of the serum was not increased, while the linolic acid content was the same as that found in normal subjects. These findings indicate a possible reason for the low iodine number of the fatty acids of the serum in cases of eczema and further suggest that a disturbance in the metabolism of the unsaturated fatty acids may be one of the many factors at fault in this condition.

HANSEN, Minneapolis. [AM. J. DIS. CHILD.]

INHERITANCE OF ALLERGIC DISEASE. A. S. WIENER, I. ZIEVE and J. H. FRIES, Ann. Eugenics **7**:141, 1936.

As the authors of this article point out, there seems to be no unanimity of opinion as to the mode of transmission of allergic disease. According to Cooke and Vander Veer and Spain and Cooke, allergy is transmitted as a simple mendelian dominant. In direct contrast, Adkinson maintains that her findings favor a recessive mechanism. Furthermore, Richards and Balyeat suggest that the condition is inherited as a "partial dominant." An analysis of the authors' studies of 66 complete families with 250 children, as well as of data already published, failed to support either the simple dominant or the recessive theory. The theory that allergy is transmitted as a simple mendelian dominant does not explain why more than half the pedigrees of both parents are normal. The theory that the mechanism is recessive is refuted by the existence of pedigrees of families in which both parents are affected yet some of the children are normal. The authors present for consideration a new theory of heredity of allergic disease. According to this theory, allergic disease is transmitted by means of a single pair of allelomorphic genes, *H* and *h*, with *h* determining allergy and *H* representing the contrasting normal gene. Three different genotypes are possible:

1. Genotype *HH*—pure normal.

2. Genotype *hh*—pure allergic. Persons of this genotype show symptoms of allergic disease before the age of 10 years.

3. Genotype *Hh*. The majority of persons of this type remain apparently normal throughout life, although they transmit the abnormal gene *h*. The rest, depending on environmental conditions, will manifest allergic diseases, but the symptoms will not appear until after puberty. The existence of two sorts of allergic persons is supported by the bimodal distribution when cases are classified according to the age of the patient at the time of onset. Moreover, statistical analysis of the authors' own findings in studies of families and of data previously published lends additional support to the theory. One finding that remains to be explained is the excess of boys over girls among those in whom allergic disease develops before puberty.

WIENER, Brooklyn. [ARCH. PATH.]

SCHÜLLER-CHRISTIAN'S DISEASE. F. R. B. ATKINSON, Brit. J. Child. Dis. **34**:28 (Jan.-March) 1937.

Moreau believes that to the triad of defects in the bones, exophthalmos and diabetes insipidus a fourth symptom should be added, namely, arrest of development ending in dwarfism.

Synonyms of this disease include xanthomatosis, lipoid granulomatosis, lipoid histiocytosis, lipoidosis and hypophysial reticuloendotheliosis.

Hand in 1893 published the first certain case of the disease but did not recognize that he was dealing with a new clinical entity.

Atkinson has collected 103 instances from the literature and discusses briefly the symptomatology and pathology of the disease and theories as to its possible

pathogenesis. The view as to its etiology that is now most popular is that it is a disorder of the lipoid metabolism, especially by the production of hypercholesteremia.

Boys are much more often affected than girls, and in the largest number of cases the condition occurs between the ages of 2 and 8 years.

Some patients slowly recover without any treatment, the deficiencies in the bones filling in. In others the gaps in the bones are never filled up, but otherwise the patient is in good health. Others die of cachexia or intercurrent disease.

Removal of fat from the diet and roentgen therapy of the affected regions seem to give the most promising results in the way of treatment.

LANGMANN, New York. [AM. J. DIS. CHILD.]

THE VEGETATIVE NERVOUS SYSTEM IN SCLERODERMA. J. RUSSETZKI, Gaz. d. hôp. **110**:381 (March 24) 1937.

The author has found that in cases of scleroderma during the stage of edema the involved areas show an altered dermatographia and that during the second (vasodilatation) phase this phenomenon is diminished. In the atrophic stage only white dermographia is obtained, and the pilomotor reaction is diminished. The oculocardiac reflex remains normal.

KAJDI, Baltimore. [AM. J. DIS. CHILD.]

PATHOGENESIS OF ERYTHEMA NODOSUM. C. DEMURTAS, Méd. inf. **8**:134 (May) 1937.

There are four opinions as to the pathogenesis of erythema nodosum: 1. It is a disease of itself, like the other exanthems of childhood. 2. It is a clinical manifestation of rheumatic fever. 3. It is related to tuberculosis, being either the result of a direct action of the tubercle bacillus or a manifestation of allergy to tuberculin. 4. It is a syndrome found in association with various infections, such as tuberculosis, syphilis, acute arthritis, pneumococcemia and gonococcemia.

An epidemic occurred in a boarding school, which led Demurtas to believe that tuberculosis is definitely the cause of the condition. One boy, aged 15, contracted acute pulmonary tuberculosis with cavity formation and died. Three other students who roomed with him came down with erythema nodosum. One of these students had tracheobronchial adenitis; a second, pleurisy with effusion, and the third, probable pulmonary tuberculosis. Each of these children showed a positive reaction to tuberculin. None of the other children in the school had erythema nodosum.

CUTANEOUS DYSTROPHY AND OBESITY OF ADRENAL ORIGIN. M. ACQUA, Méd. inf. **8**:148 (May) 1937.

Acqua reports the case of a boy of 8 years who showed an area of cutaneous dystrophy about the mouth; there were associated desquamation, scars and erythema. At first congenital syphilis was suspected, but treatment with mercury and arsphenamine did not relieve the condition. The child was somewhat lethargic had small genitalia and was obese, especially around the breast and gluteal region. Treatment with thyroid gland was tried and resulted in diminution of the obesity and some improvement in mental reaction; but the cutaneous condition was not affected. Acqua felt that the dysfunction probably was not related primarily to the thyroid but rather to the adrenal glands. Both the adrenal cortex and the medulla were believed to be involved. To the cortical disturbance was attributed the thyroid dysfunction and to the medullary was ascribed a dyscrasia of the sympathetic nervous system which included sialorrhea. The sialorrhea was believed responsible for the lesions of the skin. The administration of an extract of whole adrenal gland resulted in the overcoming of the abnormalities reported.

HIGGINS, Boston. [AM. J. DIS. CHILD.]

THRESHOLD OF TOLERANCE IN CUTANEOUS ECZEMA. E. LORTAT-JACOB, Paris méd. **1**:477 (May 29) 1937.

The author feels from his experience that eczema is due to a disturbance of the equilibrium of the vagosympathetic system which lowers the threshold of cutaneous sensitivity. The equilibrium may be upset by endocrine dysfunction or by a direct attack on the vagosympathetic system by an infecting organism.

LESLIE, Evanston, Ill. [AM. J. DIS. CHILD.]

FLACCID PARALYSIS FOLLOWING TREATMENT OF AMEBIC DYSENTERY WITH ACETARSONE. L. BABONNEIX, M. LÉVY and L. GOLÉ, Rev. neurol. **63**:191 (Feb.) 1935.

A 7 year old boy had severe amebic dysentery. Emetine, acetarsone and neoarsphenamine were given, and the symptoms lessened after four weeks of treatment. During the sixth week pains came on in the extremities, and extensive flaccid paralysis appeared. The authors reluctantly come to the conclusion that the large doses of acetarsone were responsible for the damage.

DAFFINEE, Boston. [AM. J. DIS. CHILD.]

A CASE OF "CUTIS LAXA IPO-ELASTICA." A. SETTI, Lattante **8**:342 (May) 1937.

A child of 6 months had a hypoelastic wrinkled skin practically from birth. The skin was soft and slightly greasy. The child was under par physically and mentally. A possible etiology for the condition is suggested by the fact that the parents were cousins and not in particularly robust health. Setti believes that *cutis laxa ipo-elastica* represents a recessive hereditary factor.

HIGGINS, Boston. [AM. J. DIS. CHILD.]

THE QUESTION OF POSITIVE FLUID IN FIRST YEAR OF SYPHILITIC INFECTION: INCIDENCE, PROGNOSIS AND THERAPY. AUGUST MATRAS, Arch. f. Dermat. u. Syph. **175**:85, 1937.

Tests of spinal fluid from 721 untreated patients with primary and early secondary (first year) syphilis gave positive results for 95 (13 per cent), of whom 64 were men and 31 women (3 in the seronegative, 11 in the seropositive primary and 81 in the early secondary stage). Three patients in the early secondary group showed clinical involvement of the cranial nerve and 1 showed early tabes dorsalis. Better results followed treatment with malaria than with arsphenamine and bismuth preparations. The author recommends malaria treatment for patients with early syphilis and positive spinal fluid.

BECKER, Chicago.

SYPHILITIC CONJUNCTIVITIS. A. ŠPANIĆ, Arch. f. Ophth. **137**:312 (June) 1937.

Severe, subacute, unilateral, chiefly infiltrating conjunctivitis associated with ipsilateral interstitial keratitis occurred in a syphilitic youth 18 years of age after the primary genital lesion. The conjunctivitis resembled trachoma but remained unchanged under antitrachomatous treatment. Pathologically, diffuse infiltration (by lymphocytes, plasma cells and polymorphonuclears, with a few epithelioid and giant cells) was seen. Under antisyphilitic treatment the disease subsided promptly.

P. C. KRONFELD. [ARCH. OPHTH.]

THE SEROLOGIC DIAGNOSIS OF TUBERCULOSIS, PARTICULARLY OF LUPUS. H. T. SCHREUS, Dermat. Ztschr. **74**:121 (Oct.) 1936.

The author has devised a specific method for sensitization of the complement in tuberculosis. In a comparison of this test with other methods a somewhat higher percentage of positive results was obtained in known active tuberculous infections. Of a considerable number of cases of lupus vulgaris, a positive serologic reaction occurred in between 20 and 25 per cent.

LEUKONYCHIA STRIATA. W. FROHN, Dermat. Ztschr. **74**:136 (Oct.) 1936.

Frohn describes 10 cases of leukonychia striata and expresses the belief that it occurs much more frequently than the reports in the literature indicate. There is no definite evidence as to its etiology, but trauma is undoubtedly a frequent cause. A predisposition to this condition may play a part.

RELATION BETWEEN ASSIMILATION OF WATER AND DERMATOSES ON THE BASIS OF TESTS OF WATER EXCRETION IN PSORIASIS, ECZEMA AND A FEW OTHER DERMATOSES (THE DIURETIC INDEX). ARMIN ACKERMANN, Dermat. Ztschr. **74**:185 (Nov.); 265 (Dec.) 1936.

As a result of a series of tests of the water metabolism, the author shows that patients with psoriasis, eczema, urticaria, scleroderma, dermatitis herpetiformis and erythroderma exfoliativum are all able to retain water. Since the renal function of all these patients was normal, this ability to retain water must have been due to changes in the tissue.

SUCCESSFUL TREATMENT OF DARIER'S DISEASE. O. DITTRICH, Dermat. Ztschr. **74**:207 (Nov.) 1936.

The author reports a case of Darier's disease in which clinical cure was accomplished by intensive medication with a gold compound (solganol B, the disodium salt of 4-sulfomethylamino-2-auromercaptobenzene-1-sulfonic acid). A total dose of 0.427 Gm. of the product was given in the course of three months. A mild erythematous eruption (aurid) developed but cleared promptly.

DETERMINATION OF ASCORBIC ACID IN THE URINE OF PATIENTS WITH LUPUS VULGARIS BY THE METHYLENE BLUE METHOD. KANEHIKO KITAMURA, Dermat. Ztschr. **74**:287 (Dec.) 1936.

The author determined the excretion of ascorbic acid in a group of patients by the methylene blue method described by Martini and Bonsignore and modified by Ammon and Hinsberg. The results were compared with those obtained by the iodine method, which proved much higher. Furthermore, the values obtained were not parallel. Preliminary treatment with hydrogen sulfide increased the values when either method was used. TAUSSIG, San Francisco.

PARALLERGIC VACCINAL EXANTHEM. R. BRANDT, Wien. klin. Wchnschr. **50**:369 (March 19) 1937.

Atypical reactions following vaccination against smallpox include those which depend on a specific allergic reaction (so-called parallergic symptoms).

Brandt describes the case of a 7 year old boy who was inoculated against smallpox and after ten days manifested a rash clinically similar to erythema multiforme. About two days later a new eruption with the general characteristics of a toxic urticarial multiform exanthem appeared.

The interval of ten days practically precludes the vaccine as the direct cause of the eruptions. Also, the evidence seems to rule out antibodies of the blood as having any important relation to smallpox vaccine. Finally, a strictly allergic reaction would have occurred sooner and appeared in the form of typical vaccine pustules.

The author believes that the exanthem occurred as a reaction to a nonspecific counterirritant present during the development of the vaccine-induced allergy. Identification of this third factor is aided by the knowledge that angina developed shortly after the vaccination.

Thus, the postvaccinal exanthem is to be considered a reaction of an organism made allergic by the vaccine to a parallergic antigen in the form of the cocci of the angina.

Brandt recommends the use of Keller's term "parallergic vaccinal exanthem" in place of the commonly used "postvaccinal exanthem" in describing a condition of this type.

ABT, Chicago. [AM. J. DIS. CHILD.]

SYRINGOMA (CALCIFIED SYRINGOMA). I. YAMASAKI, Hihu-to-Hitunyo **4**:687 (Dec.) 1936.

This article is supplemental to the author's communication of February 1935 to the same journal, which was abstracted in the ARCHIVES (**32**:647 [Oct.] 1935). The present contribution is concerned with the histologic observations in the case of the older brother of the 3 subjects in the family considered in the previous article. The author had noted at the time of the first report that some of the lesions on the face (lower eyelid) of the brother did not seem to be affected by the roentgen treatments. These were larger and more grayish than the surrounding skin and in some instances had a yellowish tinge (almost as though the lesion might be complicated by a xanthomatous process). One of these lesions was excised and subjected to histologic examination.

The microtome encountered resistance in cutting. The unstained cut section appeared grayish by reflected light, while under transmitted light its appearance varied from one of dark translucency to one of opaqueness. The microscope disclosed epithelial cysts, strands and agglomerations characteristic of syringoma in the upper and the middle layer of the cutis, but in the middle and more especially in the upper layer of the cutis, there were granules, aggregations and even dense plaquelike masses, chemical examination of which by the Kóssa, the Roehl and the Schujeninoff method indicated that calcium phosphate was present. Since the contents of the cysts showed no deposits of calcium; since the greatest density of deposition was within or immediately about the epithelial component of the tumor, and since regressive signs were most pronounced among the cell masses involved in the areas of deposition of calcium, the authors are inclined to support in their case the dystrophic theory of calcification.

This is thought to be the first case of calcified syringoma to be reported in medical literature.

BRENNAN, Chicago.

PUSTULOSIS VARIOLIFORMIS SEU VACCINIFORMIS ACUTA. R. KOOIJ, Nederl. tijdschr. v. geneesk. **81**:571 (Feb. 6) 1937.

The author reports a case of pustulosis varioliformis seu vacciniformis acuta in a boy of 7 months. No contact with children recently vaccinated against smallpox could be proved. Inoculation of the splenic pulp in the cornea of a rabbit failed to produce Guarnieri's bodies.

A CASE OF SYPHILIS CONGENITA IN THE "SECOND" GENERATION. C. GOEDHART, Nederl. tijdschr. v. geneesk. **81**:1436 (April 3) 1937.

Goedhart reports a case of proved syphilis congenita in the second generation of a grandfather who is now 42 years of age and who acquired syphilis at the age of 20. He was treated during the first year of the disease but not afterward. He now has symptoms which indicate with certainty an infection of the central nervous system: Argyll Robertson and unequal pupils. He has no other neurologic symptoms. The reactions of the blood for syphilis are all strongly positive. The Wassermann reaction of the spinal fluid is positive; the Müller, the Nonne and the Pandy reaction are all positive; the lymphocytes number 4. His wife, who is now 40 years of age and has never been treated for syphilis, has a strong positive reaction of the blood and no clinical symptoms at all (syphilis latens). She first gave birth to a 7 month baby and then to an 8 month baby, who lived for one and two weeks, respectively, and subsequently to a daughter, who is now 21 and who is suffering from taboparalysis congenita. This daughter never has been

treated for syphilis; she married a healthy man the reactions of whose blood were negative. After a miscarriage after three months she gave birth to a child with proved symptoms of syphilis congenita.

HIRSUTISM. L. MEYLER and H. HOMMES, Nederl. tijdschr. v. geneesk. **81**:1701 (April 17) 1937.

Meyler and Hommes describe a young girl with hirsutism presenting all the typical clinical features. There were excessive growth of hair and adipositas. The child looked much too old for her age, especially her face. Though 11 years of age, she was estimated by several persons who saw her lying in bed to be 20. The muscular force was considerable; the voice was deep, and the clitoris was enlarged. She was treated with large doses of an estrogenic preparation. After more than a year the girl had assumed a normal appearance; the muscular strength had decreased; the voice had a higher pitch, and the clitoris had become normal. It is pointed out that the syndrome called by most authors hirsutism is due to a hyperfunction of the adrenal cortex. This hyperfunction may have various causes; it is found, for example, in Cushing's disease. The latter name, however, should be reserved for those forms of hirsutism in which the adrenal hyperfunction is brought about by the hypophysis.

STAPHYLOCOCCUS TOXOID AS A MODE OF TREATMENT. W. A. TIMMERMAN, Nederl. tijdschr. v. geneesk. **81**:1725 (April 17) 1937.

A number of patients suffering from various conditions caused by staphylococci were treated with staphylococcus toxoid. There were favorable results in recurrent furunculosis; in various forms of acne the results were dubious. The initial dose should be small, and the dose should be increased slowly, with close observation of the reactions caused by the injections. Pyrexia and recrudescence of symptoms indicate that the dose has been too large.

CALCINOSIS UNIVERSALIS. J. J. C. P. A. ROOVERS, Nederl. tijdschr. v. geneesk. **81**:2346 (May 22) 1937.

A case is described, in a girl of 5 years, of generalized calcinosis in which recovery ensued after treatment with sodium citrate (3 Gm. a day) and calcium. No claim is made, however, from an etiologic standpoint.

SELF CLEANSING OF THE MOUTH. J. BOL, Nederl. tijdschr. v. geneesk. **81**:2496 (May 29) 1937.

Examination of the saliva of 53 persons showed a constant rise of the alkali content after ingestion of an orange or a tart apple; the quantity of saliva was raised in three fourths of the cases. This is important for the self cleansing of the mouth, a continuously increased amount of saliva with raised alkalinity providing a more efficient neutralization of the caries-producing acids. This is not the case with the large quantities of alkali applied in cleansing the mouth with tooth paste, which impair the self-cleansing powers and damage the teeth and gums. VAN CREVELD, Amsterdam, Netherlands. [AM. J. DIS. CHILD.]

Society Transactions

PHILADELPHIA DERMATOLOGICAL SOCIETY

FRANK C. KNOWLES, M.D., *Chairman*

Feb. 18, 1938

THOMAS BUTTERWORTH, M.D., *Secretary*

Striae Hypertrophicae Symmetricae Juvenilis. Presented by DR. MORRIS MARKOWITZ.

M. F., a Negress aged 12 years, presents numerous flesh-colored elevated striae, 2 or 3 inches (from 5 to 7.5 cm.) long, arranged transversely and symmetrically on the outer aspects of the thighs. The condition had its onset three years ago in an unknown manner.

DISCUSSION

DR. ROBERT L. GILMAN: I do not think the name describes the morphologic picture particularly well; the important point is whether or not the condition is Cushing's syndrome.

DR. VAUGHN C. GARNER: It seems to me open to question whether the lesions are actually hypertrophic simply because they are elevated. Striae atrophicae are often elevated, and I should call these lesions striae atrophicae rather than striae hypertrophicae.

DR. FRED D. WEIDMAN: It appears from the section that the elevation is due to a dense collagenous tissue, the kind one sees in linear nevi. The relation of this lesion to the birth of the patient is not known. The tissue is not the kind one expects in striae atrophicae, even in the early stages, when there is a little mucoid edematous type of tissue present.

Xanthelasmatosis, Associated with Hepatic Enlargement of Undetermined Nature. Presented by DR. CARROLL S. WRIGHT and DR. REUBEN FRIEDMAN.

F. W., a white man aged 50, is slightly jaundiced and presents a lemon yellow or chamois color of almost the entire face. An enormous butterfly configuration may be discerned. The discoloration extends from the nose to the cheeks, involving both upper and lower eyelids in one huge plaque. It continues posteriorly to the ears and thence downward, involving the entire neck, and finally terminates at the base of the neck posteriorly and anteriorly, in a sort of V-shaped or necklace configuration, with the apex over the manubrium sterni, where it fades away into normal skin. The supraorbital regions of the forehead and the nose, most of the circumoral region and the lower half of the chin are uninvolved. Raised somewhat nodular yellowish masses are present on both ears. On the oral mucosa the patient presents several groups of slightly raised yellowish papules (resembling Fordyce's disease) varying in size from that of a pinpoint to that of a pinhead and located about the orifice of Stensen's duct on each cheek and on the lower part of the buccal mucosa, opposite the region of the lower bicuspids. Following the onset of the disease, a number of small pigmented areas of atrophy have appeared on the legs, as well as numerous small irregular depigmented vitiliginous patches on the dorsa of the hands and the forearms. No definite diagnosis has yet been reached. A roentgenogram of the gastrointestinal and the biliary tract and of the skull showed no abnormalities. The Wassermann reaction of the blood and of the spinal fluid were negative. Biopsy of a specimen from the left axilla showed

nothing significant. The congo red test gave a faintly positive result; there was no sign of amyloidosis. Chemical analysis of the blood, including a determination of cholesterol, showed no essential abnormality. Tests for bile and urobilin in the urine were positive. Tests of the function of the gallbladder indicated only slight dysfunction. Tests of hepatic function showed marked obstructive impairment.

DISCUSSION

DR. FRED D. WEIDMAN: When I first looked at the face of this man, I thought of colloid degeneration. However, the sharp margination, particularly over the nose, and the appearance of one nodule at least on the elbow, made me think differently. The sections leave no question about the condition's being xanthoma. I doubt, though, that this is hepatosplenomegalic xanthoma of Urbach. Urbach has not nearly exhausted the complete category of lipoid disturbances which may appear on the skin, and I feel that dermatologists will never have a complete catalog of them. There is going to be a variation every time a new case of extensive xanthoma is brought to light, just as in this one tonight, and an attempt to attach a special denomination to that particular expression of xanthoma will be necessary. The logical classification awaits further knowledge of the etiologic basis of the different forms presented.

NOTE.—The patient died one week after presentation. At the postmortem examination about 5,000 cc. of fluid was found in the abdomen. The lungs presented one small yellowish nodule about 2 cm. in diameter, which was thought to be of tuberculous origin. The mediastinal glands were markedly enlarged, and on section were bluish yellow. There were several yellowish plaques on the trachea, at the level of the arch of the aorta. The liver and the spleen were twice normal size. The spleen showed two or three pinhead-sized yellowish nodules. The ventral glands of the gallbladder and the pancreas were greatly enlarged and on section bluish yellow. The cause of death was not determined.

Pityriasis Rosea, Associated with Oral Lesions. Presented by DR. J. P. GUEQUIERRE.

T. F., a white boy aged 10 years, exhibits typical pityriasis rosea, which began six days ago. He had a fever four days previously. There is a superficial eroded lesion on the right buccal mucosa, which has regressed during the last four days.

DISCUSSION

DR. FRED D. WEIDMAN: Most dermatologists, observing an open and shut case of pityriasis rosea, do not look into the mouth. I think all of us are convinced of the change in the picture of pityriasis rosea. It is different from what it used to be. If that is the case, why should there not be oral manifestations of it now?

DR. HERMAN BEERMAN: I should like to take exception to the statement that dermatologists have not been looking into mouths enough. In the clinic with which I am associated every patient is examined thoroughly with regard to the mucous membranes, whether he has pityriasis rosea or not, and I am sure Dr. Greenbaum has been following the same procedure. I think these oral lesions are a new finding and not something which Dr. Guequierre has happened to see.

DR. J. P. GUEQUIERRE: In 3 of 8 cases of pityriasis rosea that I have observed in the past week and a half there have been oral lesions. I do not know whether these mucosal lesions are pityriasis rosea. All except 1 of the patients with oral lesions have been adults.

Lymphogranuloma Venereum. Presented by DR. LEON HUGH WARREN (by invitation).

J. H., a Negro aged 32, was presented before this society in January 1938 (ARCH. DERMAT. & SYPH. **38**:158 [July] 1938). In addition to the data given last

month, the smear of pus showed no Donovan bodies or actinomyces granules. The guinea pig inoculated four weeks ago continues in good health, and autopsy will be performed two weeks hence. The biopsy showed chronic granulation tissue. Treatment consisting of administration of sulfanilamide tablets in a dose of 10 grains (0.65 Gm.) three times a day after meals has produced approximately 20 per cent improvement, the first improvement or remission since the onset of the disease.

DISCUSSION

DR. SIGMUND S. GREENBAUM: I have used sulfanilamide in 3 cases of discharging sinuses; in all it has been definitely helpful but not curative. A marked decrease in the purulent discharge from the sinuses generally occurs, and the patients say it is the best medicine they have had since the onset of their disease.

Neurogenic Sarcoma. Presented by DR. CARROLL S. WRIGHT.

J. B., a white man aged 71, when admitted to the hospital presented two reddish blue rounded elevated and rather firm lesions on the right foot, one on the instep and one anteriorly on the ankle. The lesions were excised by electrosurgical means. He now has several new growths on the medial surface of the ankle. There is slight swelling of the involved leg.

DISCUSSION

DR. J. P. GUEQUIERRE: Two years ago I removed the lesion on the anterior aspect of the ankle. The section was reported to show neurogenic sarcoma. The roentgenologic and the surgical department could not account for the swelling of the leg. Elastic bandages are causing it to subside gradually. I believe there is a small lesion developing at one side of the ankle. I am going to remove it for histologic examination. I realize that neurogenic sarcoma does recur. Nothing has developed at the sites of the original lesions.

DR. FRED D. WEIDMAN: I have seen neurogenic sarcoma of the bone with involvement of the medullary cavity. Were roentgenograms made of the bone?

DR. J. P. GUEQUIERRE: I do not remember whether the bones were examined roentgenologically. I remember that there was nothing relevant in the report.

Alopecia Universalis and Leukoderma Acquisitum Centrifugum. Presented by Dr. J. P. GUEQUIERRE and DR. K. I. FREEMAN, Toronto, Canada (by invitation).

C. M., a white youth aged 19, in June 1934 noticed about five patches of alopecia on the back of his head, the largest the size of a quarter. During the summer there was a regrowth of hair. In April 1935 the hair on his head suddenly began to fall out, and he became completely bald within one week. Eight months ago the pubic hair fell out suddenly within five days. He does not recall ever having had hair in the axillas, on the chest or on the extremities. The areas of leukoderma have been of the same number, shape and size as long as he can remember. There is now complete absence of hair on the scalp, the face and the trunk—including the axillas and the pubic region—and on the extremities. Circular areas of loss of pigment with a pigmented nevus in the center of each, varying in diameter from 1 to 6 cm., are distributed on the abdomen and the chest. Some pigmented nevi without areas of depigmentation are present, but all areas of leukoderma have the central brown "mole." The medical examination, including endocrinological studies, showed no abnormality. The cholesterol content of the blood was 163 mg. per hundred cubic centimeters and the basal metabolic rate was + 22 per cent. The Kolmer, the Kahn and the Eagle test were negative. Histologic examination of one of the leukodermic patches showed simply a pigmented nevus surrounded by an area of loss of pigment.

DISCUSSION

DR. ABRAM STRAUSS: I had a girl patient with a picture similar to this one. She had endocrine disturbance along with the alopecia areata, which this patient may be considered to have if it is assumed that the vitiligo is of endocrine origin. Every time the hair returned, severe acne and eczema of the hands would develop. When the hair fell out, the acne and eczema of the hands would clear.

DR. K. I. FREEMAN, Toronto, Canada (by invitation): An endocrine examination was made and nothing abnormal found, though the basal metabolic rate is +22 per cent. The areas of vitiligo with pigmented nevi in the center were limited to the nipple line on the left, and at first we thought of their being supernumerary nipples.

A Case for Diagnosis (Rosacea-Like Tuberculid of Lewandowsky?). Presented by DR. VAUGHN C. GARNER.

M. M., a white woman aged 52, presents an aggregation of minute brownish yellow papules with erythema and scaling on the middle third of her face. The condition has persisted for a year. Serologic studies and a blood count gave normal results. The reaction to old tuberculin was strongly positive. Roentgenologic examination of the chest showed evidence of a healed tuberculous process in the apex of the left lung. The patient has been given three intravenous injections of a gold preparation; there has been no noticeable improvement to date.

DISCUSSION

DR. SIGMUND S. GREENBAUM: Is the tuberculin test of any significance in such cases?

DR. VAUGHN C. GARNER: I was under the impression that patients with this condition are anergic and was surprised to find the test in this patient so strongly positive.

Dermatitis Herpetiformis; Arsenical Keratosis. Presented by DR. J. P. GUEQUIERRE.

G. deG., a white woman aged 35, states that fourteen months ago an extremely itchy red patchy eruption developed. She went to a hospital, where a diagnosis of dermatitis herpetiformis was made. She now presents a generalized hyperpigmentation with accentuation in the axillas and the groins and on the neck. The skin in certain areas shows slight lichenification. There are numerous scattered discrete raised hyperkeratotic nodules and papules. There are no keratoses of the palms and soles. There are many small excoriated flat papules. The blood count was essentially normal.

DISCUSSION

DR. FRED D. WEIDMAN: There is a peculiar sooty black color, as if there were an intermixture of stove polish in the pigmentation. It makes one think of a metallic intermixture. Have there been any local applications of mercury? Could this be a local pigmentation with mercury or with bismuth?

Vitiligo. Exfoliative Dermatitis (Gold?). Presented by DR. CARROLL S. WRIGHT.

S. B., a white man aged 61, presents an eruption of vitiligo scattered over his entire body surface, the surrounding skin showing hyperpigmentation. There are mild inflammation and exfoliation of the shoulders and the upper parts of the arms. In July 1937 a "rash" consisting of small "abscesses" appeared on the lower part of the abdomen, after the administration at a hospital of "injections into the veins" for a patchy vitiligo of the face. Shortly thereafter generalized peeling of the skin developed. Examination of the blood showed 97 mg. of sugar and 25 mg. of urea per hundred cubic centimeters. Urinalysis showed no abnormality except occult blood. The blood count showed moderate anemia.

DISCUSSION

DR. ROBERT L. GILMAN: This case bears out my opinion that if an advantageous effect is obtained from gold therapy in vitiligo, it must be obtained through the intervention of a dermatitis.

DR. FRED D. WEIDMAN: Which came first—the pigmentation or the vitiligo?

DR. ROBERT L. GILMAN: The vitiligo; he was treated with the gold preparation for it.

DR. REUBEN FRIEDMAN: This patient received an intravenous injection, and shortly thereafter pruritus developed. After the second intravenous injection, a week later, a moist, oozing dermatitis developed about the pubic region; to this little or no attention was paid. After four more intravenous injections at weekly intervals, a widespread oozing pruritic dermatitis developed, and the patient was hospitalized for five weeks, with no improvement. In January 1938 he had a dermatitis involving the entire body, with innumerable moist, oozing excoriations over the back, the chest and both upper extremities; this was associated with severe secondary pyoderma. He remained at the hospital several weeks and showed some clinical improvement when discharged. He has been out of the hospital about three weeks. It is my impression that this patient received intravenous gold therapy. So far as the effect on the vitiliginous patches is concerned, the patch over the right lower jaw, which was the first to appear, remained unchanged for a year; shortly after the institution of the intravenous therapy for the cure of this patch, new patches of vitiligo started and have continued to develop.

Telangiectatic Lupus Erythematosus. Presented by DR. ROBERT L. GILMAN.

A. S., a white man aged 27, presents on both cheeks and near the ears grouped blotchy reticulated telangiectasia. Occasionally vesicles are noted on the cheeks. There is no atrophy, scaling or plugging. There is some telangiectasia about the nose, and the patient believes he had an attack of "barber's itch" on both cheeks five years ago, at the sites of the present outbreak. There is a light port wine stain over the nuchal region.

DISCUSSION

DR. VAUGHN C. GARNER: I agree with the diagnosis.

DR. ROBERT L. GILMAN: I have not yet treated the man—purposely. In 1 case I used gold therapy, with limited success, and I do not propose to use it in this one. I shall use solid carbon dioxide.

DR. J. P. GUEQUIERRE: I have seen good results with bismuth therapy in a case in which the manifestations were similar.

Lupus Erythematosus of the Lips. Presented by DR. J. M. SCHILDKRAUT, Trenton, N. J.

A. P., a white man aged 35, has slate blue lip margins. Both lips are covered with an adherent thin silvery scale. Superficial fissures and erosions are present. The condition began about seven years ago, when he noticed swelling, cracking and peeling of both lips. He has been treated for exfoliative cheilitis with 200 roentgens of radiation in divided doses and a cream containing 1 per cent resorcinol and 1 per cent salicylic acid. There was no improvement during this therapy.

DISCUSSION

(All present agreed with the diagnosis.)

NOTE.—In the past month a typical patch of lupus erythematosus, about the size of a dime, has developed in front of the left ear, confirming the diagnosis made of the condition on the lips.

CHICAGO DERMATOLOGICAL SOCIETY

OTTO H. FOERSTER, M.D., *President*

Feb. 16, 1938

H. RATTNER, M.D., *Secretary*

Lichen Planus Atrophicus et Sclerosus. Presented by DR. OLIVER S. ORMSBY.

L. C. C., a married woman aged 47, states that small white lesions developed on the chest near the left clavicle in the summer of 1936. New lesions developed in the vicinity and elsewhere during the next several months. There were no subjective sensations.

There are patches of variable size below the clavicles, on the back of the neck and in the left cubital area. Patches are made up of flat white papules which vary in size from that of a pinhead to that of a match head. They are slightly umbilicated, and each has from one to five black points. These are either hyperkeratotic plugs or openings from which plugs have fallen. Individual discrete papules are present in addition to the patches.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: In spite of the fact that greater authorities than I think this condition is closely related to lichen planus, I think it is related to the scleroderma group. In 3 patients I have studied the process, and it was primarily sclerotic from the beginning. I believe it is more closely related to scleroderma guttatum than to lichen planus.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. W. H. Goeckerman and I, in an unpublished study of the clinical and histologic changes in about 10 cases of lichen sclerosus et atrophicus, decided that this condition was probably a disease entity, admitting that it presents both features of lichen planus and scleroderma-like changes. The histologic picture shows an atrophic process which closely resembles true kraurosis vulvae, with which it has been confused clinically in the English literature. It may at times be impossible to distinguish histologically between lichen sclerosus et atrophicus and kraurosis vulvae. The histologic changes seen in morphea also may simulate those of lichen sclerosus et atrophicus.

DR. OLIVER S. ORMSBY: This condition is a rare form of lichen planus characterized by irregular flat-topped shining white papules, each presenting on its surface one or several black horny comedo-like plugs or minute beadlike depressions, former sites of these horny plugs. The papules are ivory white or mother-of-pearl color. They often coalesce to form plaques, but even then the individual papules can be distinguished. The eruption is usually not extensive and often occurs in the sites seen today. Its resemblance to morphoea guttata is somewhat close, but it can be distinguished both clinically and histologically. It was interesting to hear Dr. Nomland say that he feels the condition is more nearly allied to morphea than to lichen planus. The opinion of most observers is that it is a rare form of lichen planus. The horny black plugs on the surface of the papules do not occur in morphoea guttata, and the lesions are more distinctly papular. I reported a group of 6 cases of this disease in 1910 (*J. A. M. A.* **55**:901 [Sept. 10] 1910) and have seen numerous examples since that time.

I have observed 1 case of dermatitis lichenoides chronica atrophicans, the disease originally described by J. Csillag (Dermatitis lichenoides chronica atrophicans, in Neisser, A., and Jacobi, E.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1909, p. 147). In this case, which was reported by Fred Wise and Bedford Shelmire (Chronic Atrophic Lichenoid Dermatitis [Csillag], ARCH. DERMAT. & SYPH. **18**:178 [Aug.] 1928), there was extensive involvement of the cutaneous surface and, while there was a resemblance to lichen planus atrophicus et sclerosus, the characteristic horny plugs were not present on the surface of the

papules and the histologic changes more closely resembled those in scleroderma. I believe lichen planus atrophicus et sclerosus is a distinct clinical entity and a variety of lichen planus and that it usually can be readily recognized.

Calcification in Scar Tissue. Presented by DR. F. E. SENEAR.

L. M., a man aged 54, sustained an injury to the left leg, and extensive scar tissue resulted. About one and one-half years ago he fell, and as a result of this injury an ulcer developed in the scar tissue. Within recent months a hard substance has formed in the granulation tissue of the ulcerative area. Eventually this reached the surface, and removal of a small piece showed that calcification was occurring in the ulcerated area. A number of spicules of "bone" have broken through the base of the ulcer and have been removed, but the process of formation has continued, and at present large spicules of the calcified material are found at both the upper and the lower portion of the ulcer.

Xanthoma Juvenile. Presented by DR. OLIVER S. ORMSBY.

F. C., a girl aged 2½ years, presents an eruption which began at the age of 3 weeks. When she was shown before this society one year ago (ARCH. DERMAT. & SYPH. **36**:207 [July] 1937), there was a generalized eruption.

The patient is shown at this time to demonstrate the change in the lesions. No new ones have developed during the year, and practically all the older ones are changing their character. They are becoming more flat, and the color is changing from bright yellow to tan. A large number have been reduced to the normal level of the skin and show a brown discoloration.

Xanthoma Diabeticorum. Presented by DR. OLIVER S. ORMSBY.

T. H., a man aged 45, had a cutaneous disease of eighteen months' duration when he was examined early in January. Shortly after its onset the Wassermann reaction was reported to be positive. A series of injections of arsphenamine was given, without effect on the lesions. At a later date hemotherapy was employed, without result.

There was a generalized eruption consisting of lemon-colored raised hemispherical papules the size of a pinhead and slightly larger. These were grouped into aggregations of from two to eight. The lesions were most numerous on the arms, the sides of the chest, the buttocks, the thighs and the knees, as well as on the lower part of the abdomen. On the dorsa of the hands were a large number of lesions, and there were a few on the palms.

Examination of the urine showed a large amount of sugar. The patient was put on an antidiabetic diet and given injections of insulin.

He has used 7 units daily of the last-named preparation. The urine today shows no sugar. The patient has lost 18 pounds (8.2 Kg.). A large number of the lesions have disappeared, and those that remain are rapidly undergoing involution.

Xanthoma Multiplex. Presented by DR. OLIVER S. ORMSBY and DR. W. W. TOBIN (by invitation).

M. L., a man aged 39, presents numerous closely grouped yellow slightly elevated dome-shaped nodules about the palms, the wrists, the elbows, the eyes and the gluteal folds. The duration of the present attack is approximately one year. Ten years ago similar nodules appeared about the elbows. These persisted for almost a year, disappearing after roentgen therapy was given. The urine showed no sugar at that time.

Repeated examinations of the urine have shown no sugar and the dextrose tolerance test showed results within normal limits. The cholesterol content of the blood was greatly increased (460 mg. per hundred cubic centimeters). The Wassermann reaction was negative.

Histologic examination of a nodule showed a flattening of the epidermis, numerous xanthoma cells, a few Touton giant cells and an increased growth of connective tissue.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. H. RATTNER.

M. V., a woman aged 33, presents a lesion on the thigh of four years' duration. It began after an injury and appeared first as a tiny red area, which gradually spread peripherally until it attained its present size. On the outer surface of the right thigh there is at present a sharply outlined infiltrated plaque the size of a 5 cent piece. The center has a yellowish waxy appearance, and the border is violaceous. The surface is smooth, shiny and atrophic and covered with numerous fine telangiectases. There are no subjective symptoms.

A diagnosis of diabetes was made two years ago, but symptoms suggestive of the disease had been present for about twenty years. The diabetes has never been under control. A general physical examination revealed no abnormalities. The basal metabolic rate was +2 per cent; the sugar content of the blood was 190 mg., the cholesterol content 342 mg. and the total fatty acids 929 mg. per hundred cubic centimeters.

Histologic examination by Dr. Caro showed the walls of the blood vessels in the corium to be thickened, even to the point of occlusion. About these vessels there were mantles of infiltration composed largely of lymphocytes and histiocytes. Deep in the corium were large areas of necrobiosis in which the collagen fibers were pale, thickened and wavy and took the stain poorly. In these areas the elastic fibers were missing. Sudan III showed many small droplets of fat within and between the fibers in the areas of necrobiosis and a few droplets of fat within the cells of the infiltrate.

A Case for Diagnosis (Nevoxantho Endothelioma?). Presented by DR. E. A. OLIVER and DR. F. J. KENDRICK, Gary, Ind. (by invitation).

P. S., a boy aged 8 months, with eczema on the cheeks and eczematous patches on the body, is presented because of numerous other lesions apparently not associated with the eczema. These lesions are discrete, saffron colored, shiny, hemispherical and elevated; they vary in size from that of a pinhead to that of a pea and are located rather indiscriminately on the head and the trunk.

A biopsy has not been made as yet.

Necrobiosis Lipoidica Diabeticorum. Presented by DR. H. RATTNER.

L. J., a man aged 28, has had diabetes for fourteen years. He presents three cutaneous lesions, one on the right shin, another on the left calf and the third on the right large toe. The oldest lesion, which first appeared about seven years ago, is irregularly oval, of about 2 by 3 inches (5 by 7.5 cm.) and sharply defined. It has a glazed surface, which is mottled yellowish in the center and has a darker, reddish brown edge. The surface is scaly and slightly depressed in the center. The oval lesion on the shin followed an injury. It is poorly defined, reddish, raised, firm and indurated. There is no yellowish center or pigmented border. The lesion on the toe followed paronychia one year ago, which recurred one month ago. It is red, fairly well defined and indurated as a patch of scleroderma. There are no subjective symptoms. The lesions have always been considered by physicians to be bruises which failed to heal properly because of the diabetes. General physical examination showed no other abnormalities. Chemical analysis of the blood showed 79.6 mg. of sugar and 155.4 mg. of cholesterol per hundred cubic centimeters. Unavoidably, the tests were made after the patient had taken insulin.

Histologic examination of the lesion on the leg by Dr. Caro showed a slight cellular infiltration about the blood vessels in the corium. In several places there was slight necrobiosis, and in these areas sudan III showed small droplets of fat

within and between the swollen fibers. The lesion of the toe showed a thickened epidermis and scale, with inflammatory changes in the epidermis and the corium. There were no changes characteristic of necrobiosis lipoidica diabeticorum.

DISCUSSION

DR. CARL LAYMON, Minneapolis (by invitation): The cases of necrobiosis lipoidica diabeticorum present much the same picture as the ones which Dr. Michelson and I observed in Minneapolis. In the case in which the lesion is present on the thigh the condition is in such an early stage that definite diagnosis on clinical grounds is difficult to make. I understand that the histologic picture verified the diagnosis. The multiple lesions in the second case are characteristic.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: In Dr. Ormsby's case of juvenile xanthoma there were no endothelial giant cells histologically, and therefore the condition can be distinguished from nevoxanthoendothelioma. It is interesting to note the partial involution of the lesions during the last year, when the patient has been on a diet relatively low in fat. Juvenile xanthoma must be regarded simply as a variant of xanthoma tuberosum. There is almost always hyperlipemia, and in adults there is frequently cardiovascular disease, especially angina pectoris. Disseminate xanthomatosis, on the other hand, has lesions limited to the flexural surfaces, the pharynx and the larynx. The blood lipoids are within normal limits, and there is frequently associated diabetes insipidus. The lesions do not respond to a dietary regimen.

The case of xanthoma diabeticorum illustrates the characteristic involution of the lesions following insulin therapy and dietary measures.

For treatment in Dr. Ormsby's case of xanthoma tuberosum multiplex, I should suggest the feeding of Dragstedt's pancreatic extract (lipocaic) by mouth. M. J. Huber, G. O. Broun and A. E. Casey (Prevention of Cholesterol Arteriosclerosis in Rabbit by Use of Pancreatic Extract [Lipocaic], *Proc. Soc. Exper. Biol. & Med.* **37**:441, 1937) have recently shown that the feeding of this extract to rabbits on a diet high in cholesterol prevents the usual increase in blood lipoids and the development of atherosclerosis. The administration of insulin causes no improvement in xanthoma tuberosum, in contrast to its effect on xanthoma diabeticorum. I wish to emphasize that even among cases of xanthoma limited to the eyelids in at least 80 per cent there will be an increase in one or more of the lipoids, and in 25 per cent there will be evidence of cardiovascular disease.

In regard to Dr. Rattner's cases of necrobiosis lipoidica diabeticorum, I thought that the histologic picture was diagnostic in the case in which there is a solitary lesion.

DR. CLARK W. FINNERUD: This group of cases interests me because it is so complete. There is not much that I can add to Dr. Montgomery's discussion. Five or six weeks ago Dr. Ormsby invited me to see the patient with xanthoma diabeticorum, and at that time the patient looked like a relief map. He was practically a solid mass of nodules. It is almost inconceivable that such a marked process could so nearly disappear so quickly.

The case of xanthoma tuberosum multiplex is interesting, in that the eruption consists chiefly of small nodules of the type usually seen in cases of xanthoma diabeticorum.

DR. F. E. SENEAR: I feel that the child with one large lesion in the frontal region and several in the scalp has a condition that would be accepted clinically as nevoxanthoendothelioma, which often shows a limited number of lesions but in some cases shows so many that it approaches the appearance of juvenile xanthoma. The general appearance of the lesions in this case is much like that in a case which I observed. I feel that these 2 cases present a good contrast, showing the differences between nevoxanthoendothelioma, which I regard as a special type of juvenile xanthoma, and the latter condition itself.

DR. OLIVER S. ORMSBY: The patient with xanthoma tuberosum multiplex was seen by me ten years ago. The lesions at that time were in much the same places

as today, on the hands, the arms and the buttocks, and I gave him a moderate amount of treatment with roentgen rays. The lesions cleared, and the patient remained healed for several years. It is unusual for the tuberous variety to respond favorably to the amount of treatment given in this case.

The diabetic condition is interesting in that it has largely cleared up within about a month under treatment with insulin and proper diet. It had been present for one and one-half years, and the antisyphilitic treatment used because of the positive Wassermann reaction had no effect on the disease. The result of insulin treatment and an antidiabetic diet, however, was excellent, far better than that obtained by previous methods.

The juvenile xanthoma began in infancy in this case. It is the xanthoma tuberosum multiplex of adults. My object was to show the difference between ordinary xanthoma and nevoxanthoendothelioma (McDonagh) seen in childhood. In all cases the latter disease clears entirely within a reasonable time, while the former usually does not. This case was presented a year ago, and the lesions have undoubtedly undergone partial involution during the year. Among 122 patients recently reported on by A. B. McGraw (Juvenile Xanthoma Multiplex, *Am. J. Cancer* **18**:345 [June] 1933), of whom a large number were children, there were 15 adults in whom the disease began in childhood. It seems likely, however, that in a certain proportion of cases the disease will undergo involution. The diet in this case has not been as rigid as I should have liked, because I had to consider the nutritional requirements. I do not object to classifying nevoxanthoendothelioma as a type of juvenile xanthoma, but it is a distinct clinical entity.

DR. H. RATTNER: I think the statement that the diagnosis in my first case is to be accepted because the woman has diabetes is interesting. There have been a few reports of similar cutaneous lesions in nondiabetic patients. In fact, there is a tendency in the literature to drop the word diabeticorum from the name.

Ringworm of the Hand and the Scalp. Presented by DR. E. A. OLIVER.

W. P., a boy aged 15, presents an infiltrated lesion on the left thumb and thenar eminence which began in September on the tip of the thumb and has gradually extended peripherally until it involves the entire thumb and part of the palm; it is associated with considerable pruritus. The skin is dry, rough, scaling and pruritic. Fungi were found in scrapings from the hand. A peculiar aspect is a large annular lesion with two advancing borders encroaching on the glabrous skin of the neck although beginning in the hair of the scalp. The patient has tinea between the toes.

DISCUSSION

DR. F. E. SENEAR: About a week ago the eruption on the palmar surface looked like pustular psoriasis or acrodermatitis continua, and certainly there was nothing in the clinical picture so far as the palmar surface was concerned to suggest a diagnosis of tinea circinata. Even today I do not believe there is. The involvement on the surface of the scalp, if that is due to the same organism, is another unusual feature, since one does not often see a combination of ringworm of the scalp and of the glabrous skin. Dr. Oliver said he had not been able to demonstrate the fungus in the lesions on the scalp as yet.

Parapsoriasis Guttata with Leukoderma. Presented by DR. A. W. STILLIANS.

C. M., a boy aged 13, small for his age, a native of Bolivia who has been in the United States for two years, first noticed red pruritic papules in September 1937. When first seen, in December 1937, he complained of pruritus, and a few of the lesions were crusted. He was told to use less soap in bathing and to apply to the lesions an ointment of zinc oxide containing 3 per cent ichthammol. Since then the pruritus has decreased; there are no crusted lesions, and the papules are fewer. No study of the case has been possible because of nervousness of the patient.

On the trunk and the upper parts of the arms are a few maculopapules from 0.2 to 0.7 cm. in diameter; these are soft and vary from pink to red; some of them are oval, and they are arranged in the lines of cleavage. When the skin is wrinkled, the markings on the papules are more evident. Some of them have adherent scales at the center. The lesions are most plentiful on the sides of the thorax and about the waist, smaller numbers being present on the forearms, the thighs and the legs. There are none on the face, the neck, the scalp, the hands or feet.

In the same areas are many partly depigmented spots, not sharply defined, oval, from 0.5 to 1 cm. long and showing more vividly where the skin is deeply tanned about the waistline. They were not noticed until the eruption had been present for a time.

DISCUSSION

Dr. F. E. Senear: The description of the lesions as exceedingly pruritic and crusted does not sound characteristic of parapsoriasis. The lesions, however, have undergone involution and are difficult to see. Yet when the surface of any of them was scratched, there appeared the white scale which is characteristic of lesions of the Juliusberg type of parapsoriasis. With the scant eruption now present, it is hard to form an opinion, but I feel that the condition may be regarded as parapsoriasis. One thing occurred to me as an explanation: It seems possible that the eruption might have started as the Habermann type, this accounting for the crusting described as present at the onset, and developed into the chronic form present now. Such a sequence would serve to emphasize the relation of pityriasis lichenoides varicelliformis to parapsoriasis.

Dr. Otto H. Foerster, Milwaukee: There is a type of disease described by Juliusberg with a varicelliform early stage and an acute course, which is the equivalent of the guttate type of Brocq and of the lichenoid and psoriasiform type of Jadassohn. Leukoderma is a common feature of the Juliusberg type. In this patient the development of leukoderma is the most extensive I have seen in connection with this disease. It reminds me of leukoderma due to syphilis, which often extended down to the waist, as I saw it in Vienna, Austria, years ago. As Dr. Senear pointed out, there must have been a preceding acute exudative type of lesion to produce the crust formation present when Dr. Stillians first saw it. That would fit in well with the picture, and I agree with the diagnosis.

Dr. A. W. Stillians: When I first saw the boy and noticed the crusts, I thought the condition was pityriasis lichenoides et varioliformis acuta. The parents had not noted the vesicles. They said that when they first noted the papules they were as I saw them. They became crusted at once. The patient said that he had not scratched them; pruritus was not severe but was noticeable.

Erythema Induratum. Presented by Dr. Harry M. Hedge.

M. C. K., a woman aged 50, presents multiple brown pigmented marks on the lower parts of the legs. The disease began nine years ago. The family history is not significant. She has 3 children in their second decade of life, all living and well. Her mother is living at the age of 75; her father died at the age of 72 and her grandfather at the age of 94.

The lesions have always been on the lower parts of the legs, at the sides and the back. They are not tender to pressure; they begin as red nodules, enlarge, break down and discharge pus for a short period and then become dry, leaving an atrophic scar. There are four active lesions at this time.

Examination of the patient for tuberculosis by her family physician has been without significant results. The Mantoux test made yesterday gave a positive result. Serologic examination was negative. Examination of the blood showed 4,750,000 erythrocytes and 4,500 leukocytes.

A Case for Diagnosis (Rosacea-Like Tuberculid of Lewandowsky?). Presented by Dr. E. P. Zeisler.

This patient, a woman aged 29, has marked edema of the entire face and a papular eruption of the forehead, the cheeks and the chin, of several years' duration. Her general health has been excellent, and there are no symptoms suggestive of tuberculosis. The basal metabolic rate is + 12 per cent, and myxedema can be ruled out. The lesions consist of soft minute reddish brown papules, most prominent on the chin. There is no associated seborrhea, telangiectasia or redness of the nose.

The histologic picture of a specimen from a lesion of the chin was not characteristic, showing no tuberculoid infiltration but mainly a collection of lymphocytes in the corium. There were no giant cells. In the differential diagnosis one must consider lupus miliaris disseminatus faciei, papular sarcoid of Boeck and acnitis, in addition to rosacea.

Treatment with an arsenical internally and two ¼ skin unit doses of roentgen radiation has resulted in some improvement in the eruption but no change in the edema.

Tuberculosis Cutis (Scrofuloderma, Sarcoid and Lichen Scrofulosorum). Presented by Dr. Theodore Cornbleet.

L. T., a Mexican boy aged 7 years, has been ill for two years. Eighteen months ago the glands of the neck became enlarged. One of them broke down, to leave a draining sinus with an unhealthy, purplish outlet on the skin. Nine months ago lesions developed on the leg and enlarged until at present there are three or four from 2 to 4 cm. in diameter; they are relatively superficial, though indurated, and have fairly sharp borders. The center of one lesion became slightly depressed and atrophic.

Several months ago a group of pinhead-sized and slightly larger papules and nodules appeared on the left foot. These are of a tawny color, relatively deep and indolent.

There is some dulness over the upper lobe of the left lung. The child appears ill.

DISCUSSION

Dr. Hamilton Montgomery, Rochester, Minn.: Dr. Hedge's case of erythema induratum presents a classic picture. The histologic section in Dr. Zeisler's case simply shows a nonspecific lymphocytic infiltrate in the cutis. In the histologic study of rosacea-like tuberculid of Lewandowsky it may be necessary to make thirty or more sections through the specimen before one can demonstrate enough epithelioid tubercles to warrant the diagnosis of tuberculosis. In some instances the histologic picture remains nonspecific. Clinically, I could not be sure of the diagnosis in this case. I think further studies, including further sections, are indicated.

The Mexican boy presented by Dr. Cornbleet illustrates the multitudinous forms that cutaneous tuberculosis may represent in the same subject from scrofuloderma to various forms of hematogenous tuberculosis. At first glance, the extensive ulceration and the nodules suggested the possibility in differential diagnosis of lazarine leprosy, such as may be seen in Mexicans and South Americans. The histologic picture was definitely that of hematogenous tuberculosis and not that of tuberculoid leprosy.

Dr. H. R. Foerster, Milwaukee: In Dr. Zeisler's case I wonder whether the edematous process may not be a streptococcic type of solid edema and the eruption an associated bacterid, although clinically the appearance is more that of Lewandowsky tuberculid than of bacterid.

Dr. E. P. Zeisler: I had hoped the discussion would throw more light on the case. I think the case is unique, presenting solid edema of the face associated with a papular eruption of unknown origin. I inquired whether there had been

attacks of erysipelas on the face, which the patient denied. Apparently some pathologic process is causing a persistent blocking of the lymphatic vessels, which is not the ordinary picture of a tuberculid.

DR. THEODORE CORNBLEET: These patients with multiple types of tuberculosis of the skin are ideal subjects for studies in immunity. The state of the disease at various sites and at different times may vary enough to account for changes in the response of the skin. It may be that once the pattern for a kind of eruption is established, that form persists. At another time, when the nutrition, the nervous balance or the permeability is changed, another eruptive pattern may be evoked. The Mantoux test with a 1: 10,000 dilution gave a positive result last month, but a negative one two days ago.

The scrofuloderma would be apt to produce a positive reaction to tuberculin, whereas the sarcoid might tend to neutralize this result. Then, of course, lichen scrofulosorum should play a role in the response to the tuberculin test. One should do quantitative tuberculin tests near the sites of the different kinds of lesions from time to time. In that way one could see the influence of time and of place.

Pemphigus. Presented by DR. M. H. EBERT and DR. A. SLEPYAN (by invitation).

R. F., a man aged 25, states that about eight weeks ago he noticed mild bilateral conjunctivitis, which readily responded to treatment. Two weeks after its onset, small blebs appeared in the mouth. A diagnosis of trench mouth was made at the time. Two weeks later an eruption appeared which was called chickenpox. After two weeks, during which blebs continuously appeared, he was brought to the hospital. He feels much better than the clinical findings would indicate.

Over the entire body, avoiding the hands and the feet, are scattered bullae arising on normal skin and varying in size from that of a bean to that of a hen's egg. Most of the bullae are broken and present an angry red base with a pale gray border. In a few of the ruptured blebs new bullae have arisen. Some of the smaller lesions present a striking picture resembling that of herpes iris. Some of the larger lesions of the extremities have become confluent, leaving large oozing patches.

Many pea-sized blebs are found on the tongue. In the past few days the patient has complained of hoarseness.

DISCUSSION

DR. THEODORE CORNBLEET: The character of the eruption has changed a great deal during the last three weeks. Prior to that time remarkable iris lesions made up of concentric bullae and all arising from normal skin separated the component elements. While the patient was in fairly good condition, I entertained the idea that he might have erythema multiforme and Duhring's disease. Dermatitis herpetiformis suggested itself because of the severe pruritus. In the last few days the skin has become more widely involved, and the constitutional state is alarming. In spite of my past impressions, I now think this man has pemphigus.

DR. E. A. OLIVER: In some cases in which the condition is of this type, it is difficult in the early stages to arrive at a correct diagnosis. The disease is probably pemphigus, but it is sometimes necessary to rule out bullous toxic erythema. To make matters still more complicated, J. V. Klauder has recently published an interesting paper in the ARCHIVES (Ectodermosis Erosiva Pluriorificialis: Its Resemblance to Human Form of Foot and Mouth Disease and Its Relation to Erythema Exsudativum Multiforme, ARCH. DERMAT. & SYPH. **36**:1067 [Nov.] 1937). That condition might be considered here.

DR. H. RATTNER: I should like to report another case of pemphigus in which sulfanilamide therapy was not successful. I think the picture in the case presented today was typical of erythema multiforme two weeks ago.

DR. MARCUS R. CARO: I should like to say a few words about the case of pemphigus which was the subject of my recent report (Pemphigus: Treatment with Sulfanilamide; Preliminary Report, ARCH. DERMAT. & SYPH. **37**:196 [Feb.] 1938). The patient showed spectacular improvement when treatment with sulfanilamide was begun and remained almost free from lesions while she consumed nearly a thousand tablets. About three months ago, however, a sudden drop in the hemoglobin content of the blood and in the erythrocyte count made it necessary to stop the sulfanilamide treatment. The pemphigus became progressively worse. On two occasions I attempted to resume treatment, but each time there was a severe urticarial reaction after one tablet of sulfanilamide. At present I am giving the patient injections of human convalescent streptococcus serum, and again there has been considerable improvement in her condition, but the response has not been as rapid as it was to sulfanilamide.

DR. M. H. EBERT: When I first came on the dermatologic service at the Cook County Hospital, I had a pretty good idea that I could differentiate herpetiform pemphigus and bullous multiform erythema. Greater experience has made me less confident. My impression is that this patient's condition is pemphigus. I agree that ten days or two weeks ago it suggested bullous multiform erythema of the annular type. However, there were bullae on perfectly normal skin; there had been no let-up in the disease, and the oral lesions were so marked that I made a diagnosis of pemphigus. I think the criterion which has been established, that if the patient dies the disease is pemphigus, is a rather poor one. Undoubtedly a number of conditions are lumped together as pemphigus. It is to be hoped that more scientific methods of differentiation may be evolved.

A Case for Diagnosis (Pigmentation of the Skin). Presented by DR. E. A. OLIVER.

L. L., a Negress aged 24, consulted a physician a year ago because of drowsiness. Serologic tests of the blood gave a positive result. She was given six or eight injections of neoarsphenamine at four or five day intervals. After the second injection the present pigmentation appeared and has remained since that time. She takes occasional doses of sal hepatica. A Kahn test showed 50 per cent and a Wassermann test with cholesterolized antigen 75 per cent complement fixation. The anterior and the posterior portions of both legs are the sites of mottled pigmentation occurring in areas varying in size from that of a dime to that of a quarter. The lower part of the trunk is involved to some extent.

DISCUSSION

DR. E. A. OLIVER: I feel that this case is probably one of fixed eruption due to neoarsphenamine, because of the persistent pigmentation ever since the second injection. To prove this clinically, of course, one should give the patient another injection of neoarsphenamine. I have not succeeded in inducing her to take more but hope to do so and will report on the result. I showed her because I know of no cases of this type of fixed eruption that have been presented here recently.

Melanosis (Postinflammatory). Presented by DR. E. P. ZEISLER.

This patient, a physician aged 43, since last summer has had pigmentation of the forehead and the temples. Preceding this there was some inflammatory change.

He states that he has used a hair tonic and some preparation containing petrolatum and has been repeatedly exposed to sunlight. There is a possibility of irritation from a hat band.

There are no general symptoms, and lymphoblastoma can be definitely excluded.

Examination of a biopsy specimen by Dr. Becker showed changes suggestive of lupus erythematosus, although the clinical appearance does not coincide with this diagnosis.

DISCUSSION

DR. S. W. BECKER: I had an opportunity to study this man briefly a week or two ago, and I questioned him relative to the use of any substance which might produce this inflammation. He said he had used no perfumed material but had used some petrolatum. He thought the eruption might be due to his hat band. I thought the condition might be of the type seen in industry, which L. M. Wieder reported a few years ago (Occupational Melanosis, ARCH. DERMAT. & SYPH. **25**:624 [April] 1932). The histologic study showed that melanin in the histiocytes and in the epidermis produced the pigmentation. There seemed to be atrophy of the epidermis and some changes at the epidermodermal junction such as are sometimes seen in lupus erythematosus. I suggested applying the hat band to the skin, as well as some petrolatum, and following the application with ultraviolet irradiation. The condition falls in the class of postinflammatory melanoses, a classification which does not exclude lupus erythematosus as the original eruption. The plugging could be explained on the basis of follicular plugging like that seen in lupus erythematosus. I think further observation and study will be necessary before a diagnosis can be made of this condition.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic picture presented all the features of lupus erythematosus, and clinically the changes are consistent with this diagnosis. There were definite atrophy and keratotic plugging of the hair follicles. The intensive pigmentation of the skin is unusual for lupus erythematosus but has been described. Poikiloderma of Civatte, which has been regarded as war melanosis of Riehl or occupational tar melanosis, shows a much more marked inflammatory reaction in the cutis than was evident histologically in this case.

DR. CLARK W. FINNERUD: As Dr. Ormsby remarked while the patient was being examined, it certainly pays to observe every case closely, because changes can be seen on close examination of this patient which might easily be overlooked. I should like to add that this case illustrates the fact that it pays to study histologically all cases in which the diagnosis is questionable. It did not enter my mind that this condition was lupus erythematosus until I saw the section and noticed that all the characteristic changes described in the paper by W. H. Goeckerman and H. Montgomery (Lupus Erythematosus, ARCH. DERMAT. & SYPH. **25**:304 [Feb.] 1932) were present. If one could not see the patient, I am sure one would be inclined rather definitely to make a diagnosis of lupus erythematosus from the section alone. The clinical picture is not as classic as the histologic picture, but when the two are put together I feel that, atypical as the clinical manifestations are, the condition is lupus erythematosus and probably not a melanosis of other character.

DR. H. R. FOERSTER, Milwaukee: My impression is that this condition may be similar to one of the war melanoses that were described by E. Hoffmann and R. Habermann (Arzneiliche und gewerbliche Dermatosen durch Kriegsersatzmittel [Vaseline, Schmieröl und eigenartige Melanodermatitiden], *Deutsche med. Wchnschr.* **44**:261, 1918) and others. In the cases they observed the condition resulted from contact with unpurified oils, greases and petrolatum made from coal tar, substituted for petroleum products and acting in association with sunlight; that is, the hydrocarbon served as a photosensitizer and predisposed the patient to an inflammatory reaction followed by pigmentation, atrophy and follicular keratoses. Riehl's melanosis was not a reaction of photosensitization but a similar hyperpigmentation, the consequence of nutritional disturbances due to war substitutes in food, and, while in all Riehl's cases there was a predominance of pigmentation on the face, it was present also on covered parts of the body. This picture may occur in lupus erythematosus, but I think it unusual to have so much pigmentation in that disease.

DR. OTTO H. FOERSTER, Milwaukee: It seems to me that there is atrophy especially of the left lower temporal region extending over the zygoma and an inflammatory change that one could associate clinically with lupus erythematosus.

That, fitted in with the histologic picture, bears out what Dr. Becker has found. I should consider this condition as probably an unusual form of lupus erythematosus.

DR. E. P. ZEISLER: I should be inclined to agree with Dr. H. R. Foerster's opinion: that the condition is not lupus erythematosus.

Argyria Under Treatment. Presented by DR. ERDOS BROWN (by invitation) for DR. A. W. STILLIANS.

V. B., an American woman aged 21, when 6 years of age, was given treatment with mild protein silver every day, sometimes twice a day, because of frequent colds and bronchitis. Her sister and brother, 8 and 4 years old, respectively, were given the same treatment less often but never changed color.

After two years of this regimen the mother noticed an abnormal color of the patient's feet. The physician explained this as due to bad circulation and insisted on continuing the silver treatment. In another month the change in color had become general. The physician then made a diagnosis of cardiac disease and advised baths and avoidance of exercise.

Ten years later the diagnosis of argyria was made. Injection treatment with the method of Lawless and Stillians was begun in May 1937 and has been given about once a week since.

The entire body is dark gray, the color being somewhat deeper on the hands than elsewhere. As a result of treatment, the face is covered with depigmented spots, in spite of the effort to keep the injections close together. A strip about 2 cm. wide and 15 cm. long down the left side of the neck has been treated, and in this area there is no mottling.

It has been found that stainless steel needles are suitable for this work and leave no such marks as do ordinary steel needles. They give much less trouble and are less expensive than the platinum needles formerly thought necessary.

DISCUSSION

DR. A. W. STILLIANS: Our idea in presenting this case was to show the result of hard work and patience on the part of both physician and patient and to show the patch on the neck, on which there were much better results than were obtained on the face, the troublesome mottling being eliminated.

DR. OLIVER S. ORMSBY: I presented a case a few months ago in which a similar condition followed long-continued use of mild protein silver in the nose (ARCH. DERMAT. & SYPH. **37**:692 [April] 1938). These cases call attention to the danger of using a local application of silver for an extended period.

Multiple Basal Cell Epitheliomatosis. Presented by DR. HARRY M. HEDGE.

F. E. A., a man aged 69, has had a red patch of about 11 by 7 cm. in the lower part of the dorsal region for the past twenty years. This has been diagnosed repeatedly as psoriasis. The border is a little elevated, and the entire patch is deep red and smooth but not ulcerated. It does not increase in size now but at first grew a little larger each year. About six or eight months ago many granuloma-like lesions appeared over the body; these grew appreciably from time to time. They range in diameter from 0.5 to 2 cm. The Wassermann and the Kahn test gave negative results. Examination of the urine showed no abnormality. Examination of the blood showed 4,325,000 erythrocytes, and 12,000 leukocytes, and a practically normal differential count. The lesions are friable and bleed frequently.

Histologic examination showed basal cell epithelioma.

DISCUSSION

DR. OLIVER S. ORMSBY: I think this case is a classic example of the disease. It is now well known that these patches resembling psoriasis or Paget's disease are epitheliomatous but are often overlooked for years, being accepted as psoriasis.

The threadlike elevated margin is present in all and is diagnostic. Some years ago Dr. O. S. Ormsby and I recorded a case (ARCH. DERMAT. & SYPH. **12**:144 [July] 1925) in which there were a large number of psoriasiform lesions with threadlike margins; in some of these nodules developed. The histologic picture of such a patch showed the margin to be a basal cell epithelioma and the nodule a prickle cell epithelioma, while the scaling center showed merely dyskeratosis. In most of these cases the lesions remain benign and may be overlooked until seen by one familiar with that type of lesion.

DR. FREDERICK R. SCHMIDT: I think it is important to remember what Drs. Mitchell and Ormsby brought out, that these little growths do show malignant tendencies at times. Many years ago Arndt was the first to point out their resemblance to new growths of the ileum, called carcinoids. In the European literature they are so described. Fuhs and I studied many reports of cases in the literature and observed cases at the different Viennese clinics; in several there was malignant degeneration, so the condition should not always be considered as purely basal cell epithelioma.

DR. CHESTER A. DOTY, Detroit: In a case which recently came to my attention two adjoining lesions on the side of the face clinically appeared to be basal cell epithelioma. A section from one showed basal and from the other squamous cell epithelioma. I feel that it is essential to secure sections of all the lesions.

DR. HARRY M. HEDGE: It must be borne in mind that these lesions become metastatic and may change as time progresses from the basal to the prickle cell type and may show ever increasing malignancy.

Bilateral Herpes Zoster. Presented by DR. H. RATTNER and DR. THEODORE CORNBLEET.

This article will appear in full in a later issue of the Archives.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi). Presented by DR. F. E. SENEAR and DR. MARCUS R. CARO.

R. T., an Italian girl aged 16, has had varicose veins on the right leg since early childhood and has always noticed that her right leg and thigh were larger than the left. About four months ago a patch developed on the outer surface of the right ankle. At the time of the first examination this was a thickly crusted dermatitis. The crusting improved rapidly after the application of a bland ointment.

At present there is an irregularly outlined palm-sized purplish patch on the outer surface of the right ankle, lying over a network of varicose veins. Within this patch are areas of atrophy and poorly defined areas covered by a thin dry scale.

Histologic examination showed the changes to lie chiefly in the corium. In the upper part of the corium the blood vessels were markedly dilated; there were many newly formed vessels, considerable proliferation of fibroblasts and histiocytes and much free hemorrhage into the tissues. Deeper in the corium the same changes were present about the larger vessels, and there were many granules of brown pigment, which were shown to be blood pigment by Perles' prussian blue reaction.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I hesitated to accept the diagnosis as presented in this case, because of the age of the patient, the location of the lesions and the microscopic picture. Professor Krenn once stated to me that a diagnosis of Kaposi's sarcoma for a lesion not on the fingers or the toes must be accepted cautiously. The microscopic section showed individual features which were consistent with the diagnosis, but the whole picture does not seem correct to me.

DR. DAVID LIEBERTHAL: It is probable that trauma preceded the development of the lesion on the leg, as it looks like a contusion. Furthermore, the plaque is of considerable size, a rather rapid development for a hemorrhagic sarcoma. In regard to the histologic picture, I share the view of Dr. Michelson. The numerous hemorrhages and the cellular infiltration are the predominant features; however, no other characteristic of this disease is seen. Although I do not agree with the diagnosis, I do say that the case is interesting, and I urge continued observation of it.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic picture in this case would be consistent with the earliest microscopic changes seen in Kaposi's sarcoma but does not, in my belief, establish this diagnosis, in view of the large size and the character of the lesion clinically. With a lesion of this size, one would expect all the multiple and varied features of Kaposi's sarcoma, including areas of lymphocyte-like cells, proliferation of the cells of the capillary vessels and of histiocytes, areas of increase in connective tissue cells and other areas of hemorrhage with deposits of hemosiderin, to occur in the same section. The histologic slide shows a regular and uniform pattern of capillary vessels, together with hemorrhage and deposits of hemosiderin, which would be consistent with the presence of a vascular disturbance in this area almost since birth.

DR. MARCUS R. CARO: It is true that the picture clinically is not typical of Kaposi's sarcoma. About five years ago, however, Dr. Senear and associates presented a case (ARCH. DERMAT. & SYPH. **27**:851 [May] 1933; ibid. **34**:734 [Oct.] 1936) that was similar clinically and histologically to this one and the diagnosis in that case was accepted by several members. In the sections taken in the present case we found many newly formed blood vessels, considerable proliferation of fibroblasts and much blood pigment, all of which fit in with the histologic picture of multiple idiopathic hemorrhagic sarcoma. Further observation will be necessary, however, before a definite diagnosis can be substantiated.

Bromoderma. Presented by DR. JAMES H. MITCHELL and DR. J. R. WEBSTER (by invitation).

R. W., a Negress aged 30, complains of a recurring lesion on the right leg of four years' duration. She states that the original sore was a small "pimple" on the outer aspect of the right leg above the ankle; this enlarged, became ulcerated and finally healed. From time to time this cycle has been repeated in the same general region but not elsewhere on the body.

In 1929 she was treated at the Municipal Tuberculosis Sanitarium for pulmonary tuberculosis but was told she was cured and has not returned since. She has been troubled for some time with what she terms "indigestion" and has taken a salty medicine for this off and on for six years.

Encircling the right leg above the ankle, in a band about 3 inches (7.6 cm.) wide, are moderate somewhat atrophic scarring and increased pigmentation. On the medial aspect of the leg within this band is a well defined roughly oval lesion of about 6 by 4 cm., elevated 4 or 5 mm. above the level of the skin and with a papillomatous surface that bleeds rather easily on mild trauma. There is a small amount of purulent material on the surface, but no definite abscesses are to be found.

A roentgenogram of the chest showed a few small areas of calcification at the right hilus but no other abnormality. A Mantoux test with 0.1 c.c. of a 1:100,000 dilution of old tuberculin gave a definitely positive result. The Wassermann test gave a negative result. Serologic tests were negative. The fluorescein test of a large specimen of urine, after concentration, gave evidence of the presence of a considerable amount of bromide ion.

Histologic examination of a biopsy specimen hardened in alcohol, embedded in paraffin and sectioned and stained with hematoxylin and eosin, showed massive acanthosis with considerable edema in the epidermis and a poorly developed stratum corneum. In the upper layers of the corium there were considerable

dilatation and new formation of capillaries and a rather diffuse cellular infiltrate made up of young connective tissue cells, lymphocytes, an occasional plasma cell and polymorphonuclear leukocytes. There were no characteristic arrangement of these cells and no microscopic abscesses. No blastomycetes were observed in the section.

DISCUSSION

DR. WILLIAM ALLEN PUSEY: As I examined this patient and agreed with the diagnosis, it occurred to me that I do not see bromoderma and iododerma as much as I used to. These conditions are not common now in private practice, and I wonder if that is another illustration of changing fashion in disease, as with blastomycosis, or if the conditions are occurring less frequently than formerly.

DR. THEODORE CORNBLEET: I have had under study for several months the excretion of bromides by the skin and have made many interesting observations. I have had 1 woman whose lesions are similar to those in this case and in whom the secretion of bromide from the skin is definitely altered. It appears that the epithelium in these persons holds more bromides than that of normal persons—so much so that the preponderance of bromide coming through the skin actually is attached to the epithelium instead of coming through in solution in the sweat.

DR. J. R. WEBSTER (by invitation): I have little to add. We felt that from a purely clinical standpoint an absolute diagnosis was not particularly feasible in this case, but after investigation it seemed that the most probable clinical diagnosis, namely, bromoderma, was substantiated. The absence of blastomycetes in fresh and in fixed and stained preparations spoke against blastomycosis; the diffuse and nonspecific character of the granulation tissue spoke against tuberculosis, in spite of the unverified history of pulmonary tuberculosis and the positive Mantoux test, and the negative Wassermann reaction plus the fact that for four years the condition had been present only in this localized area spoke against syphilis. The finding of large amounts of bromide ion in the urine and the fact that the patient had been taking a salty medication for years seemed to make it a certainty that she had been ingesting bromides, although for this presentation we were unable to obtain an analysis of the medicine in question. These points taken together definitely substantiated the diagnosis of bromoderma.

Syphiloderm (Late) Resembling Erythema Annulare Centrifugum. Presented by DR. M. H. EBERT.

E. A., a woman aged 43, states that she has had recurring ring circles on the backs of the hands, the arms and the shoulders since childhood. No change in sensation is noted. The lesions start as pea-sized nodules, clear in the center, and spread peripherally. A ring may persist for two or three months. She was married when 15 years old. Her first 2 children are living and well. The third pregnancy terminated in a miscarriage at three months.

The lesions are distributed on the backs of the hands, the arms and the shoulders. The majority are half-circles made up by coalescence of split pea-sized nodules. The large semicircles are 3 inches (7.5 cm.) in diameter. The smaller ones are coin sized.

Histologic examination of sections from one of the nodules showed a perivascular infiltrate in the upper part of the corium. The small arteries showed endothelial proliferation, and the cells were epithelial cells, lymphocytes and a few plasma cells. The Wassermann reaction was 4 plus.

Tertiary Syphilis (Extensive). Presented by DR. THEODORE CORNBLEET and DR. H. RATTNER.

C. J., a man aged 74, was admitted to the hospital because of an eruption on almost the entire right side of the body and head and about the left elbow.

The history was rather vague, but the patient stated that the eruption began about five years ago with an open lesion of the right ankle. This healed, and new

lesions occurred in the interim, involving the entire leg and thigh. Two years after the first lesion on the ankle, new ones appeared on the left elbow, which took about one year to heal. About one year ago he noticed the same type of lesions on the forehead and the face (right side).

Examination shows an atrophic process on the right thigh and leg and the right side of the head, spreading to the left side of the head, and many atrophic lesions near the left elbow. The atrophic lesions are preceded by deep-seated processes, apparently of an infectious nature. Many of these active processes are found within the borders of the atrophic lesions.

The Wassermann reaction on two occasions was negative; examination of the urine showed no abnormality; examination of the blood showed 40 mg. of urea nitrogen and 2.66 mg. of creatinine per hundred cubic centimeters. The patient has been treated with potassium iodide and mercury rubs since Jan. 30, 1938.

Histologic examination of a lesion on the face showed atrophy and flattening of the epidermis. The upper part of the epidermis was edematous and contained widely dilated lymphatic vessels. The collagen fibers here stained poorly, and the elastic fibers were missing. A loose cellular infiltration in this zone with sudan III stain was seen to contain many droplets of fat. Some of the blood vessels were markedly thickened, even to the point of occlusion.

Histologic examination of the ulcer on the leg showed chronic inflammation.

DISCUSSION

DR. W. W. TOBIN (by invitation): Within the past year I have seen 2 patients with lesions almost identical with those in Dr. Ebert's case. In both cases the lesions were urticarial and of gyrate pattern, resembling erythema centrifugum. However, they proved to be late syphiloderms when further examined.

DR. M. H. EBERT: Had I known there would be such a remarkable demonstration, perhaps I should not have asked this patient to come today. She was shown not because her condition is unique but because it is novel. She states that the lesions have been recurring since childhood. Evidently she is not telling the truth, or else she originally had some other type of eruption. The histologic section shows the condition to be syphilis. The lesions apparently leave no atrophic areas as they progress. There are other interesting features: the lesions have been confined to the upper extremities, if her story can be believed.

DR. THEODORE CORNBLEET: I was rather uncertain as to the correct diagnosis in my case, although I had in mind, of course, tertiary syphilid; but the condition was rather remarkable for its great extent and particularly because it was confined for the most part to only one side. I imagine the older dermatologists have seen conditions like the present one in days gone by. Even at the Cook County Hospital, I have never seen anything approaching this for extent of involvement. This man has been under antisyphilitic treatment for several weeks but so far shows only moderate improvement.

Granuloma Annulare. Presented by DR. TIBOR BENEDEK (by invitation).

W. L., a man aged 58, has had destructive arthritis for the last five years.

The patient appears well nourished. He has recurrently painful swollen joints. He is disabled. All the organs are normal, including the heart, the tones of which are distant but regular with no murmur. The rhythm is regular. The rate is 80. There is no evidence of cardiac enlargement.

About November 1937 he observed small brownish red papules on the skin between the left first and second metacarpal bones, near the edge of the web. While this lesion was growing, several similar lesions appeared. When he was seen for the first time, on Feb. 1, 1938, he showed a 25 mm. horseshoe-like lesion between the left first and second metacarpals near the web, with an elevated border consisting of brownish red papules 2 or 3 mm. in diameter and a depressed

center. He has two other annular lesions, 10 or 12 mm. in diameter, along the left second metacarpal bone. Four similar lesions are to be seen on the back of the right hand, the smallest one of which is 5 mm. and the largest 13 mm. in diameter. They are annular brownish red papules, depressed in the center. The nape of the neck between the ears, from the border of the scalp down to the seventh vertebra, is covered with numerous discrete annular or gyriform papular lesions from 3 to 10 mm. in diameter. The color is bright brownish red; the infiltration is minimal.

The urine was normal. Examination of the blood, including a differential count, showed no essential abnormality. An intracutaneous tuberculin test with original tuberculin in a dilution of 1:10,000 showed after forty-eight hours a 15 by 15 mm. red infiltrated nodule. This reaction was unchanged after five days.

At histologic examination of an old lesion (about four months) the epidermis showed normal pegs, a marked granular layer and stratum lucidum and hyperkeratosis. Now and then a few wandering cells could be seen in the stratum spinosum. The center of the section consisted of a large infiltrate reaching from the deeper layers of the corium to the rete and involving the papillary bodies. In the upper layer of the stratum reticulare there were a number of new capillaries; in the deeper layer the vessels were markedly dilated and showed a thickened wall. The sharply limited infiltrate consisted of fibroblasts and epithelioid cells. There were no plasma cells or polymorphonuclears, but a few giant cells were present. In the center of the clearcut infiltrate there was no coagulation necrosis, but the degeneration of the collagenous tissue was evident. Within the infiltrate the elastic tissue was destroyed.

Histologic examination of a young lesion showed no change in the epidermis. In the corium the stratum papillare showed a slight infiltration with a few wandering cells. There were many newly formed capillaries. The vessels were dilated. The walls were not thickened, but they were surrounded with round cell infiltration. The section showed two well defined nodular infiltrations consisting of epithelioid cells, monocytes and fibroblasts. The infiltrate did not reach the rete, and it was not yet as dense as that in the older lesion. There was degeneration of the collagenous tissue within the infiltrates but no necrosis. Around the sebaceous and coil glands there was a marked infiltration of epithelioid cells, round cells and monocytes. Collagenous tissue was degenerated, and elastic tissue was destroyed within the infiltrate. In Ziehl-Neelsen preparation neither lesion showed tubercle bacilli.

DISCUSSION

DR. CLARK W. FINNERUD: The picture in this case is absolutely identical with that in one I presented a year ago (ARCH. DERMAT. & SYPH. **36**:635 [Sept.] 1937). Most of the members will recall it: that of a physician who had lesions in exactly the same areas. Histologically the picture was much the same. The condition is not granuloma annulare or lichen planus but some form of tuberculosis, and I should like to know how to classify it. The newer lesion of the two shown in sections was of classic tuberculoid structure; the other one was merely suggestive. I should like to hear from Dr. Michelson on the clinical classification of this eruption. It is some form of tuberculid, but I do not know what form.

DR. H. E. MICHELSON, Minneapolis: This is a difficult lesion to diagnose. On analysis the eruption consists of various-sized rings, none of them large, and they seem to be spreading peripherally. The centers seem to have some atrophy. I considered lichen planus, granuloma annulare and sarcoid. I thought the absence of individual papules and the color were against the diagnosis of lichen planus. The size of the lesions and the microscopic section were against granuloma annulare. I thought most of the elements necessary for a diagnosis of miliary sarcoid, annularly arranged, were present. The section of the early lesion showed tuberculoid structure, but this is consistent with the diagnosis of sarcoid, and the older lesion was sufficiently characteristic to justify that diagnosis.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: This case is probably of the type which has brought confusion in the literature between annular sarcoid and granuloma annulare and probably corresponds to those cases in which granuloma annulare has been described as having epithelioid cells and giant cells and, therefore, as being of tuberculous origin. In the biopsy of the older lesion there was a suggestion of beginning necrosis of the connective tissue, as seen in granuloma annulare. However, I agree with Drs. Finnerud and Michelson that definite epithelioid cells and giant cells resulting in fairly typical tubercle formation were present. I should therefore be inclined to the diagnosis of an unusual form of annular sarcoid. In no case of typical granuloma annulare that I have studied histologically have I been able to demonstrate definite tubercle formation.

DR. A. W. STILLIANS: I am grateful for the discussion. I have heard something I never heard before.

Pruritus (Generalized); Enlarged Prostate; Urinary Retention. Presented by DR. THEODORE CORNBLEET.

H. A., a man aged 72, was well until four weeks ago, when he entered the hospital because of generalized pruritus. There was no eruption. The pruritus had been intractable except when temporary relief was obtained by bathing in hot water.

Examination shows a dry, sallow skin with many scratch marks. The abdomen is pendulous below the umbilicus. Rectal examination showed the prostate to be markedly enlarged throughout. Yellowish material loaded with white blood cells could be expressed. With a catheter 600 cc. of residual urine was removed.

The Wassermann test gave a negative result on two occasions. The urine was turbid, with many white blood cells. Examination of the blood showed 94 mg. of urea nitrogen, 6 mg. of creatinine and 94 mg. of sugar (during fasting) per hundred cubic centimeters.

DISCUSSION

DR. DAVID LIEBERTHAL: The presentation of Dr. Cornbleet's patient has been interesting as well as instructive. Long before tests for allergy came into use, the search for causative factors in various cutaneous diseases necessitated sometimes extensive examinations. This still holds good in a large percentage of cases in which the tests for allergy do not give any positive results. As an example of this I may cite a case of intensive toxic erythematobullous dermatitis of the thighs and the axillas in which the cause was not ascertained and the disease was resistant to my efforts at treatment until the patient intimated that he felt some urethral irritation and at times discharge. A urologic examination disclosed chronic nonspecific prostatitis. After a short course of treatment by a urologist the dermatitis subsided rapidly.

DR. THEODORE CORNBLEET: At first blush one might think of just senile pruritus in such a case, and that may well be present. There is generalized pruritus in a senile man, but I have watched several such patients who have undergone prostatectomy and then experienced improvement in the pruritus. I saw one improve without prostatectomy from the mere use of an indwelling catheter; the condition of his skin improved as well as his pruritus. Although it is difficult to prove, I feel that there is a connection between the enlarged prostate, urinary retention and dry skin with pruritus in some cases of senile pruritus. Most patients with this condition have increased retention of nitrogen and one may look on their state as preuremia. Many years may elapse before they arrive at a terminal stage.

Tinea Microsporina Erythematosquamosa, Followed by Microsporids, Caused by Microsporum Equinum (Bodin). Presented by DR. TIBOR BENEDEK (by invitation).

Folliculitis. Presented by DR. CLARK W. FINNERUD.

HAMILTON MONTGOMERY, M.D., *President*

March 16, 1938

H. RATTNER, M.D., *Secretary*

Leiomyoma Cutis. Presented by DR. OLIVER S. ORMSBY.

A. T. F., a woman aged 32, presents a widespread eruption of the skin which has been present for fourteen years and occurs on covered parts of the body. The lesions are variously sized nodules, grouped in some areas and discrete in others. The eruption began on the right thigh and gradually spread to the right leg and the back and later to the left arm. There has been continuous gradual development of the lesions up to the present time.

The lesions are firm pinkish yellow raised variously sized nodules. Some are aggregated into palm-sized groups, while others are irregularly scattered over the surface. On the upper part of the back are three elevated tumor-like lesions the size of half a cherry. Extreme pain occurs when the skin becomes chilled, and the lesions are painful on pressure.

Histologic examination by Dr. Ebert showed that the tumor mass occupied the entire thickness of the corium, except for a band of collagen which separated the new growth from the epidermis. The tumor was made up of parallel bands which took the same stain as smooth muscle. These bands ran at various angles and were made up of long fibers with the type of nucleus characteristic of smooth muscle. In the body of the tumor the collagen had been largely replaced. At the margins, tongues of tumor tissue had pressed the bundles of collagen apart.

DISCUSSION

DR. OTTO H. FOERSTER, Milwaukee: The members are indebted to Dr. Ormsby for acquainting us with a new and unusual clinical manifestation of leiomyoma cutis. Instead of limitation of the lesions to small areas, this patient presents a most extensive distribution, with groups of lesions of classic type and, on the shoulders, several large nodular lesions. The latter are an unusual manifestation, and the distribution is far more extensive than in any other case known to me.

DR. E. A. OLIVER: Several cases of leiomyoma cutis have been presented before this society, but none in which the lesions have been so widespread.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic picture is typical in this case and shows the origin of the smooth muscle bundles from the arrectores pilorum. It sometimes is necessary to make many sections to demonstrate this origin. I recently saw a woman aged 32 who had a solitary painful nodule over the right knee which clinically suggested glomus tumor or leiomyoma. The histologic picture was that of low grade leiomyosarcoma, and there was no evidence of a connection of the muscle bundles with the arrectores pilorum. It was felt that there might have been abnormal proliferation of the muscular coats of the vessels of a glomus tumor.

DR. OLIVER S. ORMSBY: This case was presented because the disease is uncommon and because the lesions are unusually extensive. Dr. Mitchell and I presented the first example of this disease before this society fourteen years ago (ARCH. DERMAT. & SYPH. **9**:656 [May] 1924). In our histologic study, in which was included material from 2 patients, we demonstrated the fact that the tumors originate in the arrectores pilorum. Some observers have suggested that the musculature of the walls of the blood vessels furnishes the point of origin. Because of the extreme pain in the lesions, we attempted to demonstrate the presence of nerve fibers, but at that time stains were not available for that purpose. It was our conclusion that pressure on the nerve fibers by the dense connective tissue causes the pain. In the early stages, when the lesions are soft, no pain occurs,

but later, as they become larger and harden, pain develops. All the patients note the pain during atmospheric changes and when the lesions are palpated. With new stains available, it is our hope that more success will follow examination for nerve fibers. No treatment other than surgical removal or destruction of the lesion otherwise has been successful. Refrigeration with solid carbon dioxide reduces the size of and the pain in the lesions. Roentgen and radium irradiation have been of no service. Surgical procedure in a case in which the involvement is so widespread as this is not practicable. I suggest the removal of the larger lesions surgically and the relief of pain in the others with carbon dioxide refrigeration.

DR. M. H. EBERT: In discussing this case with me, Dr. Vincent O'Conor, a urologist, said that smooth muscle tumors or leiomyomas of the bladder are not uncommon and not infrequently degenerate into a sarcoma. He asked me if this degeneration occurred in the skin. I had never heard of its occurrence. K. Zieler (*Arch. f. Dermat. u. Syph.* **105**:211, 1910), however, reported 1 case of sarcomatous degeneration in an elderly woman.

Lupus Vulgaris. Presented by DR. E. A. OLIVER.

M. W., a woman aged 34, states that in September 1937 she noticed a small papule on the left side of the forehead, just above the eyebrow. This gradually enlarged, until at present it is approximately ½ inch (1.3 cm.) long and ¼ inch (0.6 cm.) wide and is surrounded by a group of small deep-seated reddish brown papules. The lesion is dark red and on diascopic pressure yields an apple jelly color. It is shown today as an early lesion of lupus vulgaris.

A Case for Diagnosis (Sarcoid?). Presented by DR. H. RATTNER.

A. N., a butcher aged 29, presents a group of lesions of two and one-half years' duration on the flexor surface of the right forearm, just above the wrist. The lesions are deep-seated nodules varying in size from that of a pea to that of a coin, and through the skin they appear faintly purplish. In two areas the overlying skin is atrophic, shiny, depressed and covered with tiny telangiectatic vessels. The whole group covers an area 2 by 3 inches (5 by 7.6 cm.). There are no subjective symptoms. According to the history, the first lesion began as a tiny red spot and slowly enlarged; then smaller new lesions appeared around it. Past treatment has consisted of application of local remedies and of two fractional doses of roentgen radiation.

The Wassermann test gave a negative reaction; the blood count showed 8 per cent eosinophils and was otherwise normal.

Histologic examination by Dr. Caro showed a thin loose scale covering a flattened atrophic epidermis. In one small area the epidermis was disorganized by the invasion of cells from the corium, and the scale was parakeratotic. In the subpapillary layer of the corium the blood vessels were surrounded by densely packed mantles of infiltration composed largely of lymphocytes and a few epithelioid cells. Extending deeply into the corium were several poorly defined zones consisting of a large central area of necrosis with many epithelioid cells and connective tissue cells and a wide border of lymphocytes and connective tissue cells. Within these zones lay many disorganized sweat glands and thickened blood vessels. No tubercle bacilli were found.

DISCUSSION OF PAPERS BY DRS. OLIVER AND RATTNER

DR. CLARK W. FINNERUD: These 2 cases were interesting. I think Dr. Oliver's case is properly classed as one of tuberculosis cutis. I do not know that the condition is lupus vulgaris, because of the clinical appearance of the lesions and the short duration.

I think the patient Dr. Rattner presented shows the histologic picture of infectious granuloma, but in spite of the presence of an occasional epithelioid cell in the section, I do not believe the condition is sarcoid. I do not know what it is.

DR. E. A. OLIVER: This patient was first seen this morning at my office; no biopsy has as yet been made. Because of the isolation of the lesion, its short existence and the definite apple jelly color under pressure, early lupus vulgaris was offered as the diagnosis. So far, I see no reason to change my diagnosis.

DR. H. RATTNER: I presented my case for diagnosis, because I did not know where to classify it and I thought that the histologic picture suggested sarcoid more than anything else.

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. F. E. SENEAR and DR. H. SHELLOW (by invitation).

M. A. D., a man aged 30, states that an eruption developed six years ago, beginning on the shoulders and gradually spreading over the entire body. Pruritus was present constantly, at times being intense. Several months ago the glands in the groin broke down and have been draining. From time to time patches of dermatitis developed; these became painful and moist. Despite treatment with ointments and internal medication by more than a dozen physicians, as well as many roentgen treatments, the condition has become progressively worse. Recently there have been progressive weakness and swelling of the ankles.

Examination shows erythroderma, generalized except for a few isolated nummular areas. The involved parts are infiltrated and covered by fine fragmented branny scales. Here and there over the trunk are indurated deep nodules the size of a small nut and larger and irregularly outlined infiltrated plaques, many of which are eczematous and covered with serous and hemorrhagic crusts. The plaques are definitely raised above the surrounding skin. The glands are generally enlarged and palpable; those in the inguinal region have broken down, and sinuses have formed and are draining. The palms and the soles are affected, showing deep vesicles in poorly outlined patches, as well as scaling and fissuring. The picture here is not unlike that of dermatophytosis. There are destructive changes in the nails, and the nail folds are involved with a deep vesicular eruption.

Serologic tests of the blood gave negative results. The first examination of the blood showed 4,670,000 erythrocytes, 14.75 Gm. of hemoglobin and 20,000 leukocytes; a few days later there were 13,950 leukocytes. The differential count showed a normal number of platelets, 73 per cent polymorphonuclear neutrophils, 13 per cent lymphocytes, 9 per cent monocytes and 5 per cent eosinophils. No pathologic cells were seen. The erythrocytes showed practically normal characteristics. Examination of aspirated sternal marrow showed 2 per cent fat (yellow) cells, 47 per cent plasma cells, 9 per cent "myeloid" cells and 42 per cent "red" cells.

Histologic examination of a section from the skin showed a thick parakeratotic scale with slight crusting in the center. The epidermis showed considerable acanthosis and fusion of the rete pegs, and there was much intracellular edema. In the upper part of the corium there was a diffuse infiltration composed of lymphocytes, macrophages, plasma cells, a few large mononuclear cells and eosinophils and a few mitotic figures. The blood vessels in the upper half of the corium were surrounded by dense mantles of the same types of cells.

DISCUSSION

DR. OTTO H. FOERSTER, Milwaukee: The immediate impression given by the widespread erythroderma, the diffuse infiltration and several subcutaneous plaques is of the pretumorous stage of mycosis fungoides. As time goes on, one may expect the gradual or sudden development of the classic features of this disease. It is now well known that mycosis fungoides not infrequently remains masked, perhaps for years, under the clinical picture of the plaque type of Brocq's erythroderma. The clear areas with convoluted borders on the knees attracted my attention, for such areas, I think, are seen often as part of the clinical picture of mycosis fungoides.

DR. CLARK W. FINNERUD: I have seen sections made in a number of cases of early mycosis fungoides, and the changes presented in these sections today are perfectly compatible with such a diagnosis, in spite of the fact that there is no marked multiplicity of cell types in the infiltrate. It is not possible to say with absolute certainty that one of the other lymphoblastic diseases will not develop. I should like to hear what Dr. Montgomery thinks of these sections.

DR. OLIVER S. ORMSBY: I have shown at least 4 patients with lymphoblastic erythroderma before this society. A certain proportion of these patients when first seen show no change in the blood, which later shows leukemia. In these patients the skin presents a characteristic dusky red appearance, sometimes associated with fine scaling. In the present case the picture differs in that there are areas or plaques of definite infiltration, and the color is different. Clinically, the symptoms are those of a pretumorous stage of mycosis fungoides.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: It is important to note that 9 per cent monocytes were found in the blood. J. F. Fraser and H. J. Schwartz (ARCH. DERMAT. & SYPH. **33**:1 [Jan.] 1936) have shown that mycosis fungoides is a disease of the reticuloendothelial system. C. G. Lane and A. M. Greenwood (ARCH. DERMAT. & SYPH. **27**:643 [April] 1933) reported a case of Kaposi's sarcoma associated with mycosis fungoides. Julius Doerffel (ARCH. DERMAT. & SYPH. **26**:608 [Oct.] 1932) has stated the belief that Kaposi's sarcoma is a disease of the reticuloendothelial system in which there is an increase in the number of monocytes in the blood. Thus, there is justification for including monocytic leukemia of Schilling under the general term lymphoblastoma. Dr. C. H. Watkins and I recently reported 3 cases of monocytic leukemia of Schilling (*Arch. Int. Med.* **60**:51 [July] 1937) in which there were cutaneous manifestations, the disease in 1 case starting out as mycosis fungoides. In the last six months I have observed 4 cases of exfoliative dermatitis due to monocytic leukemia of Schilling. H. R. Foerster in 1934 saw a woman with a general exfoliative dermatitis and the hemocytologic changes of lymphatic leukemia; later, when she was seen at the clinic, the changes were those of monocytic leukemia of Schilling, and recently, the hemocytologic picture has reverted to that of lymphatic leukemia. The histologic picture in the case presented today fails to reveal any evidence of the clumping of cells or the multiplicity of cell types with pyknosis and karyorrhexis of the individual cells usually seen in mycosis fungoides. Several of the cells show a peculiar longitudinal grooving of the nucleus which is characteristic of monocytic leukemia of Schilling. Further sections should be studied carefully under high magnification, and hemocytologic studies should be made to rule out or to establish a diagnosis of monocytic leukemia in this case.

Scleroderma-Like Lesions on the Legs (Poikiloderma?). Presented by DR. E. A. OLIVER and DR. F. J. KENDRICK, Gary, Ind. (by invitation).

E. H., a woman aged 50, was seen first eight months ago, when she had coin-sized shiny atrophic smooth slightly yellowish patches on the legs. There were a few telangiectatic vessels at the edges of the patches. Histologic examination of a specimen from one of the lesions at that time showed a sclerodermoid picture.

About three months ago an acute erythematous pruritic eruption developed suddenly on the legs, the thighs and the trunk. As the eruption subsided, small punctate pigmented lesions were left in the areas previously covered by the acute erythematous eruption.

The Wassermann reaction was negative. Complete examination of the blood and of the urine, including sugar tolerance tests, gave results within normal limits. The coagulation, the bleeding and the clotting time were normal.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The picture presented in this case is unique in my experience. There are many oval lesions, several

centimeters in diameter, that look like spider nevi and show tiny capillaries radiating from central puncta. These lesions, however, are atrophic, and adjacent thereto are other areas of guttate atrophy and of pigmentation. The pigmentation is not of the cayenne pepper type associated with Schamberg's disease. There were no lichenoid papules or areas of lichenification to suggest a diagnosis of pigmented purpuric lichenoid dermatitis of Gougerot and Blum. The clinical picture is not that of angioma serpiginosum, nor is it a severe enough process to warrant the designation of poikiloderma. The cutaneous changes might be the result of so-called war melanosis of Riehl or an occupational tar melanosis.

DR. OTTO H. FOERSTER, Milwaukee: I should like to suggest that in the differential diagnosis acrodermatitis chronica atrophicans be given consideration. The cutaneous atrophy and the small patch of scleroderma-like lesions at the knees, the vascular stasis of the hands and the feet and the cutaneous vascular ectasia elsewhere may be early manifestations of that condition.

DR. E. A. OLIVER: This patient is Dr. Kendrick's. I had not seen her previously. I do not believe the condition falls into that large group of "poikiloderma-like" dermatoses, because there is no resemblance to poikiloderma. I did note the peculiar generalized pigmentation and the scleroderma-like patches on the legs, but I have no diagnosis to offer.

Discoid Lupus Erythematosus Involving the Palpebral Conjunctiva. Presented by DR. M. H. EBERT.

D. F., a white man aged 27, has an eruption on the face. The first plaque appeared on the forehead three years ago and has since undergone involution; others have appeared. About two years ago the left lower eyelid became involved. At first the involvement disturbed the patient's vision, and he consulted an oculist, but during the past few months it has caused no discomfort. Treatment has consisted of a few intravenous injections, administration of an arsenical preparation by mouth and some roentgen therapy locally; there has been no apparent effect. The family and personal history are not significant.

There are several dull red coin-sized plaques and some adherent keratotic scaling typical of discoid lupus erythematosus on the cheeks and the temples. One lesion involves the margin of the scalp with atrophic scarring alopecia. The mouth and the lips are free. The lateral half of the left lower palpebral conjunctiva is bright red and slightly raised and is covered with dilated vessels. The lesion extends over the palpebral border in an area 5 mm. wide. The bulbar conjunctiva is slightly congested above the lesion.

DISCUSSION

DR. CLARK W. FINNERUD: A few years ago I checked on a considerable number of cases of discoid lupus erythematosus and found a large proportion in which there were lesions of the mucous membranes, particularly in the mouth. The patient ordinarily was not aware of the lesion. In tabulating lesions of the mucous membrane, O. Kren (*Arch. f. Dermat. u. Syph.* **83**:13, 1907) found that the conjunctival mucous membrane was involved in something like 3 per cent of cases of discoid lupus erythematosus, I believe, and that in something like 25 per cent there was involvement of the mouth. I have observed involvement of the conjunctiva in but 2 cases.

DR. M. H. EBERT: I thought the case was worth presenting because it prompts dermatologists to look for lesions. Had it not been for a slight congestion of the bulbar conjunctiva, I should not have found this lesion. Since Dr. C. W. Finnerud's first paper (*Arch. f. Dermat. u. Syph.* **148**:318, 1925) appeared, I have been on the lookout for mucosal lesions in discoid lupus erythematosus, and I agree that they are not uncommon in the mouth but doubt if involvement of the conjunctiva is present in 3 per cent of cases.

Melanoma. Presented by Dr. James H. Mitchell and Dr. W. W. Tobin (by invitation).

This patient, a woman aged 75, states that eight years ago a pea-sized, skin-colored elevation appeared on the right sole and became progressively darker until it was almost black. The area was excised twice but recurred each time. Several roentgen treatments produced no improvement. The area gradually enlarged and another area appeared nearby on the inner arch of the foot. For the past year the patient has been applying a corn remedy.

There are now two areas on the right foot, one on the inner aspect of the arch and the other on the sole; both are superficially ulcerated and studded with many soft brownish black papules. There is no evidence of further involvement. Subjective symptoms are pruritus and pain on pressure.

This patient is presented because of the long duration of the disease with little evidence of metastasis and for suggestions as to treatment.

DISCUSSION

Dr. E. A. Oliver: I agree with the diagnosis of melanoma but have nothing to offer in the way of treatment. I do not believe any therapy is indicated, because of the age of the patient and the chronicity of the condition.

Dr. F. E. Senear: Since lesions of this type involving the foot often pursue a rapidly unfavorable course after operative interference and in view of the fact that this lesion has shown no tendency to extend or to metastasize for many years, it is my feeling that the lesion should be left untouched.

Dr. James H. Mitchell: I shall take this occasion to report on a patient presented previously (Arch. Dermat. & Syph. **35**:764 [April] 1937, **36**:922 [Oct.] 1937). The members may recall that this patient had a black lesion on the outer margin of the foot. I treated it intensively with roentgen radiation and thought I had finally controlled it. The patient was shown at a time when there was practically no activity. Later the lesion recurred, and I found a great deal of pigmentation, which I again treated intensively, producing marked necrosis. She was seen in consultation with Dr. Ormsby, and not long afterward metastasis appeared in the groin. The last I heard was that metastases had developed in the brain, and I suppose by this time she has died.

Dr. W. W. Tobin (by invitation): In view of the patient's age and the relatively slow progress of the lesion in the past nine years, I think that the lesion should not be treated.

Submucous Hemorrhage of the Uvula with Necrosis, Following Ingestion of Acetylsalicylic Acid. Presented by Dr. M. H. Ebert.

M. M., a white man aged 45, has been taking 30 or 40 grains (from 2 to 2.6 Gm.) of acetylsalicylic acid per day for the past year. Occasionally a black and blue spot developed on the body, but five days ago a crop of them appeared, and a day later he noticed that his uvula was sore. He had an attack of herpes zoster on the right side three weeks ago.

Several subcutaneous hemorrhages, varying in size from that of a coin to that of a palm, are scattered over the trunk and the extremities. The uvula is markedly swollen and blue-black, and there is a small necrotic area on the anterior surface.

DISCUSSION

Dr. Clark W. Finnerud: I should like to mention a case I observed recently: A woman was hospitalized because of painful hematomatous swellings in the abdominal muscles and elsewhere; these were the size of a hand or larger. According to the gastroenterologists, she had been having hemorrhages in the gastrointestinal tract similar to those in the present case for many months. Careful study by hematologists ruled out various types of purpura. For years she had been taking from 8 to 20 tablets of acetylsalicylic acid daily for migraine,

and these relieved her of her pain from the hematomas. Of course, the hemorrhagic lesions kept forming. Since the ingestion of this drug was stopped, she has had no more purpuric lesions.

DR. OLIVER S. ORMSBY: The lesions in this patient are probably due to the ingestion of acetylsalicylic acid. Over a period of years I have observed a large number of cases in which hemorrhagic lesions like those present on the skin of this patient have developed during the use of acetylsalicylic acid and disappeared when its ingestion ceased. This type of lesion may be considered common and characteristic. I have never seen involvement of the mucous membrane.

DR. M. H. EBERT: Much more work must be done on this patient. When I first saw the uvula I though of scurvy, which can cause that type of hemorrhage. However, the margins of the gums were in good condition; the patient's diet was normal, and I was not satisfied that the condition was scurvy. I considered Werlhof's disease. I found that the patient had been taking much acetylsalicylic acid for a long time.

A Case for Diagnosis (Fixed Eruption). Presented by DR. M. H. EBERT.

V. M., a white man aged 45, presents a pruritic eruption of four months' duration. His personal history is irrelevant. Aside from the cutaneous disease he seems perfectly well.

Scattered over the covered parts of the body are well defined round to oval areas, slightly pinker than the normal skin and varying in size from that of a coin to that of a palm. They are not infiltrated, and a faint scale can be raised by scratching them. Small keratotic plugs in the hair follicles resemble lichen spinulosus at the margins of some of the patches. When the patches have invaded the bearded region and the scalp on the nucha, they have caused alopecia. Examination of the blood showed no abnormality. The Wassermann reaction was negative. There were no fungi in scrapings from the lesions.

Histologic examination showed slight hyperkeratosis and small areas of parakeratosis. Definite keratotic follicular plugging was seen, and there was mild acanthosis with a few small areas of edema in the rete mucosa. There was a slight perivascular infiltrate about some of the vessels in the upper part of the corium.

NOTE.—At Dr. Wile's suggestion, the patient was given a test dose of phenolphthalein, which caused erythema and some edema of some of the patches, especially on the face.

DISCUSSION

DR. CLEVELAND J. WHITE: I saw this man about two months ago and believed that his condition could be classed with the lymphoblastoma group, because of partial alopecia of the eyebrows. I was anxious to get a biopsy specimen, but he refused permission.

DR. JAMES H. MITCHELL: Some years ago I saw a patient with multiple lesions of lichen spinulosus approximately the size of a dollar. I demonstrated that these were due to taking phenolphthalein. They were exactly like the lesions over the right scapula of this patient.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic picture showed no evidence of lymphoblastoma. I favor the diagnosis of a fixed drug eruption.

DR. M. H. EBERT: I did not consider drug eruption on account of the presence of localized areas of alopecia. While the lesions look redder at times, I have seen no definite flare-up such as is seen in drug eruptions.

A Case for Diagnosis (Addison's Disease? Chloasma?). Presented by DR. CLEVELAND J. WHITE.

J. B., a white woman aged 48, was first observed about five months ago because of symmetric brownish black pigmentation on each side of the face and neck and

on the forearms, which had been present and becoming more pronounced for three months. General examination revealed no significant findings. The previous history is irrelevant except for bilateral pleuritis in 1931.

Dermatologic examination shows well demarcated areas of pigmentation in the locations mentioned. There is no pigment in the oral mucosa.

Laboratory examination showed only one feature of importance, a low hemoglobin content (73 per cent). Shadows of density were noted in the lower lobe of each lung on roentgen examination. The anemia has been corrected, and no pulmonary activity may be found on physical examination. There has been no ischemia. The blood pressure has remained within normal limits. Histologic examination showed nothing of significance.

DISCUSSION

DR. THEODORE CORNBLEET: According to the history, the amount of pigmentation was decreased when vitamin C was administered. That may be taken as some evidence for Addison's disease, yet it would not rule out chloasma. A number of observers have reported that while the administration of vitamin C does not remove all the excess pigment in some of the "pigmentoses," it is definitely useful in such diseases. The administration and withdrawal of potassium is one differential diagnostic measure which may be used in Addison's disease. An increase in the intake of this element aggravates most of the symptoms. Contrariwise, an increase in the intake of sodium chloride produces improvement.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I wish to support Dr. Cornbleet's remarks and in addition to suggest that roentgenograms be made of the adrenal glands.

A Case for Diagnosis (Epithelioma of the Tongue). Presented by DR. JAMES H. MITCHELL.

W. W., a man aged 56, was first seen in April 1928 and was treated until October of that year for tabes dorsalis. The entire tongue was covered with leukoplakia. (A photograph was presented.) The patient was not seen again until Jan. 22, 1938, at which time he had a lesion on the dorsum of the tongue in the posterior midline; this had been present for two years.

The Wassermann and the Kahn test gave negative results. Three injections of neoarsphenamine produced no effect on the lesion or on the serologic reaction. The lesion has grown slowly and has caused little discomfort except by its size and location. There has been no ulceration. The extent and the thickness of the leukoplakia have greatly decreased.

The lesion is well rounded, smooth, firm, pedunculated and about the color of the tongue. A small piece of tissue was removed by slipping a cutting loop under the free border on the left and cutting toward the center. The first biopsy was not satisfactory, and a second specimen was removed on March 12; its preparation was just finished today, and it has not been studied yet.

The first histologic examination showed in the upper, outer portion of the tumor marked and irregular benign hypertrophy of the epithelium. In the inner, deeper portion of the mass were whorls of squamous epithelial cells of low grade malignancy. The center of the mass consisted largely of plasma cells, with little stroma.

DISCUSSION

DR. CLARK W. FINNERUD: I have previously seen sections from the lesion. I must conclude that a leukoplakic area has become papillomatous and further developed into a low grade squamous cell carcinoma, which as yet is just beyond the borderline stage. If it were in my mouth, I should want it eradicated promptly.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Through the courtesy of Dr. Mitchell, I was able to study both specimens for biopsy. The first specimen showed a benign type of dyskeratosis, with the formation of spaces within the

epidermis similar to those seen in Darier's disease, and there was evidence of malignant dyskeratosis and early epitheliomatous change. The changes just described are frequently seen in the early stages of any of the precancerous dermatoses, including leukoplakia and erythroplakia.

The second specimen was more suggestive of squamous cell epithelioma. F. P. McCarthy (ARCH. DERMAT. & SYPH. **34**:612 [Oct.] 1936) reported that syphilis is frequently an etiologic factor in leukoplakia when it occurs on the tongue, especially following atrophic syphilitic glossitis. Clinically, in this case I should favor a diagnosis of squamous cell epitheloma. The histologic picture was strongly suggestive of early squamous cell epithelioma rather than of pseudoepitheliomatous hyperplasia.

DR. JAMES H. MITCHELL: I want to thank Drs. Finnerud and Montgomery for their fine spirit of cooperation. I was much interested in this case because of the difficulty of diagnosis. The clinical picture resembles that in the 2 cases of glossitis rhombica mediana recorded by J. A. Fordyce and A. B. Cannon (ARCH. DERMAT. & SYPH. **8**: 749 [Dec.] 1923). The lesions were lobulated, while in this case the lesion is smooth and single, but histologic examination of the first section showed a similar picture. The connection of leukoplakia with lesions of the central nervous system is well known. C. Levaditi expressed the belief that the virus of syphilis of the central nervous system gives the same type of sclerosing lesion on the tongue as in the central nervous system. I was not satisfied with the first section, and this new section seems definitely to demonstrate that the condition is a benign type of squamous cell epithelioma. The question whether it should be removed with the cutting loop will have to be decided by myself.

Physical Allergy in Sisters; Sensitization to Sunlight. Presented by DR. F. J. KENDRICK, Gary, Ind. (by invitation).

M. P., a girl aged 17, states that she was severely sunburned two years ago. Since that time a few moments' exposure to sunlight will cause marked erythema, which subsides in two or three hours. When she was seen yesterday, twenty minutes' exposure to sunlight produced marked erythema.

H. P., a girl aged 18, sister to M. P., had pronounced cutis marmorata on both legs.

Both patients have a livedo type of circulation of all extremities.

DISCUSSION

DR. M. H. EBERT: It is difficult to say whether the cutis marmorata type of circulation in the lower extremities of H. P. is due to a functional spasm of the deep arterial network or whether actual organic changes are present. I should be inclined to think the change is functional.

DR. FREDERICK R. SCHMIDT: Since Haxthausen published his work on light dermatoses (*Hospitalstid.* **61**:1422, 1918), a good deal of knowledge has accumulated to explain the apparent contradictions mentioned by the presenter, such as the fact that this patient reacted with erythema when exposed to sunlight but not when exposed to ultraviolet radiation. In some subjects hypersensitivity to sunlight develops only after repeated exposures of the same area of skin to the actinic ray. The wavelength plays an important role. By using a series of different colored pieces of glass to exclude the various wavelengths, it is possible to determine exactly which wavelength is at fault. Other substances such as the chlorophyll of plants, sweat, etc., affect the skin as sensitizers or catalyzers. Usually a combination of factors, often called the "exposition," is necessary to elicit a reaction. It is well known that animals fed on buckwheat in the winter are sensitive to sunlight when let out in spring.

Ulerythema Acneiforme. Presented by Dr. M. H. Ebert.

C. W., a Negress aged 50, presents a lesion of the left breast which has been present for one year, during which it has progressed slowly. She was admitted to the medical service of the Cook County Hospital because of dyspnea and edema of the legs of two years' duration. During the last two months she has been in bed at home. She has had a moderate fever.

A left-sided pleural effusion was found, and 300 cc. of straw-colored fluid was drained. The laboratory examination has not been completed. The tentative diagnosis is tuberculous pleurisy.

The cutaneous lesion occupies a crescentic area just external to the areola of the left nipple and extends two thirds of the way around it. There are four types of lesions: (1) dilated follicles filled with large comedo-like black plugs, (2) follicular papulopustules, from which yellow pus can be squeezed, (3) shallow clean-cut ulcers 3 to 6 mm. in diameter and (4) soft depressed scars, many of which have coalesced to form large scars, in one place 1 by 3 cm. in extent.

A histologic section showed a nonspecific inflammatory reaction.

DISCUSSION

Dr. M. H. Ebert: I think this condition is a dermatologic curiosity. In the first place, the presence of pleurisy and the elevation of the temperature make it necessary to consider an unusual form of tuberculosis cutis. The term ulerythema describes the curious, well demarcated, punched-out-looking scars. The progress is slow. O. Gans (Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 547) described a similar pustular lesion on the face and called it ulerythema acneiforme. In my experience it is unique in this area.

Actinomycosis. Presented by Dr. M. H. Ebert.

Carcinoma of Penis (2 Cases). Presented by Dr. H. Rattner.

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

In Connection with Organization of American Academy of Dermatology and Syphilology

Jan. 14, 1938

Detroit Dermatological Society, Hosts

George H. Belote, M.D., *President*

Thomas H. Miller, M.D., *Secretary*

Arthur E. Schiller, M.D., *Recorder*

GROUP 1

Case 1.—Disseminated Hematogenous Tuberculosis of the Lupus Tumidus Type. Presented by Dr. Franz Blumenthal, Ann Arbor, Mich., and Dr. H. Pinkus, Eloise, Mich.

E. B., a well developed and well nourished Negro aged 32, presents fifteen or twenty lesions which are symmetrically distributed on the face, the neck, the trunk, the scrotum and the extremities. They vary in diameter from several millimeters to 15 cm. and consist of indolent sharply defined soft, tumor-like plaques, elevated from 2 to 8 mm. Their surfaces are furrowed as if composed of confluent nod-

ules. The larger plaques are scaly and partly eroded in the center. The lesions resemble keloids except for their softness. A probe breaks through the surface easily. Diascopic examination reveals yellowish brown miliary nodules beneath the surface of the less pigmented parts of the lesions. The remaining examination reveals large bilateral nasal polyps and bilateral complete indirect inguinal hernia.

In 1923 the patient first noted that a plaquelike lesion of about 1 by 3 cm. was developing on the right side of the neck; it was soft but not tender. At the City of Detroit Receiving Hospital in 1925 this lesion and a similar one under the right eye were excised. Within eight months both recurred and rapidly grew to their present size. The next lesion appeared on the lower part of the right cheek in 1927, and one developed on the upper lip in 1933. Since then multiple lesions have developed on the face, the body and the extremities.

Roentgenograms of the chest showed no abnormality. The Mantoux test gave a positive result with a 1:10,000,000 dilution. The Kline exclusion test gave a negative result. Inoculation of a guinea pig produced tuberculous lymphadenitis; acid-fast bacilli were demonstrated. Histologic examination of sections from various lesions showed considerable thinning of the epidermis and the upper half of the cutis, down to the layer of the sweat glands, which were occupied by an accumulation of epithelioid tubercles with lymphoid sheaths. Numerous giant cells and often central necrosis were present. The cutaneous appendages showed destruction.

Case 2.—A Case for Diagnosis (Tuberculosis?). Presented by Dr. George Van Rhee, Dr. Claude W. Behn, Dr. John Hamlin Besancon and Dr. J. H. Cobane, Detroit.

E. M., a Negro aged 36, American, presents an exudative nodulopustular dermatitis in the central portion and on the periphery of the forehead. On the bridge of the nose several nodular lesions the size of a small pea have become crusted and healed, leaving small flat erythematous scars.

The eczematoid areas cleared after application of moist dressings, and the nodular dermatoses after administration of potassium iodide and of neoarsphenamine intravenously. The patient received 9¼ skin units of roentgen radiation.

The eruption on the face started five years ago as a small nodule on the midforehead, spread rapidly and itched mildly. Small drops of pus could be expressed from the lesions. The past history is irrelevant.

The Kahn test gave repeatedly negative results. Cultures showed no blastomycetes. The blood count showed 88 per cent hemoglobin, 4,900,000 erythrocytes and 7,600 leukocytes, with 73 per cent polymorphonuclears, 26 per cent lymphocytes and 1 per cent eosinophils. Histologic examination showed ulceration of the horny layer. In the rete there was hyperplasia, wtih down growing prolongations, and some infiltration, largely composed of lymphocytes. In the papillary layer of the corium and in the rete there was early abscess formation. No blastomycetes were seen.

Case 3.—Grouped Nodular Tuberculids (Jadassohn). Presented by Dr. Franz Blumenthal, Ann Arbor, Mich., and Dr. H. Pinkus, Eloise, Mich.

A. E., a white man aged 47, a barber, states that for two and one-half years nodular cutaneous lesions appeared mainly on the extremities. Individual lesions grew larger, the surface becoming reddened and sometimes slightly scaly. The lesions disappeared spontaneously after weeks or months, leaving pigmentation and sometimes depressed scars, while new nodules appeared in the vicinity, often resulting in the formation of a plaque spotted with pigmentation, with scars in the center and active lesions in the periphery.

The patient has suffered from measles, mumps, chickenpox, whooping cough and pneumonia. He states that he has had no venereal infection or close association with tuberculous persons and has never noticed symptoms of tuberculosis. His right hand has been crippled since he had purulent tenosynovitis after an injury one and a half years ago.

At present he has horseshoe-shaped lesions on the right temple of 1.5 and 2.5 cm. diameter; these are composed of deep cutaneous firm pea-sized nodules, are indolent and are raised 2 or 3 mm. above the surface. A similar lesion, a little more superficial, with a slightly reddened and scaly surface is present on the left scapula. A group of barely raised cutaneosubcutaneous nodules form a semicircle of 5 cm. diameter just beneath the head of the right fibula. The center of the semicircle is occupied by small depressed pigmented scars. Active nodes are separated from the scar and from each other by normal skin. The surface is brownish red and in some instances scaly or slightly atrophic.

The lesions from which biopsy specimens were removed have changed gradually. Old nodes subside, and new ones appear. At present all the old groups are enlarged by peripheral apposition, and new lesions are present on the left thigh. The nodes arise deep in the cutis and extend slowly to the surface. Physical examination showed no further evidence of tuberculosis. The patient has received roentgen treatments to the face and the legs.

The Kline exclusion test was repeatedly negative. Pirquet's test showed erythema of 1 cm. and mild infiltration after forty-eight hours; this subsided within one week. Roentgenograms of the chest showed some intensification of the descending bronchi but no recent areas of infiltration and no consolidation in either lung. There were no osseous changes in the extremities or pathologic changes in the gastrointestinal tract. Inoculation of a guinea pig gave negative results after two months.

Biopsy of a facial lesion showed cutaneous nodes of tuberculoid structure and perivascular arrangement grouped around necrobiotic centers of connective tissue, in which the elastic fibers were well preserved. Collagenous fibers were edematous, with necrosis affecting mainly the cellular elements. Inflammatory tissue consisted of epithelioid cells and some lymphocytes. Giant cells in varying numbers and occasional plasma cells were observed.

Sections from the leg showed similar nodes of tuberculoid structure, arranged mainly around the blood vessels and the sweat coils. The pathologic changes affected the entire cutis and reached down into the subcutis, growing more severe from the surface downward. There was actual necrosis of connective tissue and of fat.

The microscopic diagnosis was chronic granuloma of the skin, most likely tuberculous, combining features of sarcoid and of granuloma annulare.

Case 4.—A Case for Diagnosis. Presented by Dr. George Van Rhee, Dr. Claude W. Behn, Dr. John Hamlin Besancon and Dr. J. H. Cobane, Detroit.

N. W., a Negress aged 32, presents slightly indurated nodular lesions on the right ala and the upper lip. The surfaces of the nodules are depigmented and show rather marked telangiectasia. There are plaquelike lesions on the arms and the legs. The skin is thickened and depigmented and shows some atrophy and slight telangiectasia. The condition first appeared about one year ago, starting as a nodule the size of a small pea on the left nasal ala and gradually enlarging until most of the ala was involved. A similar lesion then developed on the right ala and on the upper lip.

The family and past history are irrelevant. The patient has been treated with sodium gold thiosulfate.

The Kahn test was negative. A blood count showed 83 per cent hemoglobin, 4,200,000 erythrocytes and 5,650 leukocytes, with 74 per cent polymorphonuclears, 21 per cent lymphocytes, 3 per cent monocytes and 2 per cent eosinophils. The basal metabolic rate was —1 per cent. Histologic examination showed lymphocytic infiltration around the lymph spaces and the hair follicles. There were dense fibrosis of the perifollicular areas and edema around the blood vessels and the hair follicles.

Case 5.—**A Case for Diagnosis.** Presented by Dr. George Van Rhee, Dr. Claude W. Behn, Dr. John Hamlin Besancon and Dr. J. H. Cobane, Detroit.

M. P., a white woman aged 62, a music teacher, complains of a small nodule on the upper part of the right arm, which resulted from the breaking of a needle during a hypodermic injection in 1922. The nodule was excised but recurred. The plaque gradually increased to about 3 by 4 inches (8 by 10 cm.), and successive crops of new lesions appeared on the back. Patches appeared on the right cheek and the lobe of the right ear about one year ago. The examination showed nodular lesions forming infiltrated pink to red plaques, which were covered with scales. In August and September 1936 many of the patches on the back and the right cheek ulcerated. A mucopurulent serum was present. Administration of sodium gold thiosulfate, ultraviolet irradiation, local injections of phenylethylhydnocarpate and a salt-free diet have not produced striking results on the whole.

Roentgenograms of the chest showed evidence of tuberculosis in childhood and calcified glands in the hili of the lungs but no evidence of active tuberculosis. Neither cultures nor inoculation of animals with the patient's blood revealed tubercle bacilli. The blood count showed 85 per cent hemoglobin, 4,260,000 erythrocytes and 5,850 leukocytes, with 75 per cent polymorphonuclears, 19 per cent lymphocytes, 1 per cent monocytes and 5 per cent eosinophils.

Case 6.—**Lupus Eythematosus Disseminatus.** Presented by Dr. R. A. C. Wollenberg, Detroit.

E. T., a farmer's daughter aged 22, states that in childhood she had an eruption which appeared each summer, usually in August, and disappeared about the time of the first frost. It appeared on the legs and then on the head, the neck and the upper extremities. Occasionally there was moderate fever.

In May 1937 the eruption appeared on the face and then spread rapidly to the neck, the upper part of the chest and the extensor surfaces of the arms and forearms; it consisted of large confluent red to grayish brown scaly macules. It improved during treatment but recurred, and she was treated at the University Hospital, Ann Arbor, Mich., in the service of Dr. Udo J. Wile. At that time the lesions were confined chiefly to the head, the neck, the upper extremities and the anterior surfaces of the lower parts of the legs. The eruption consisted of purplish, dusky erythema, with superimposed coarse scales. There were marked swelling about the eyes, puffiness of the face in general and marked conjunctivitis, with epiphora and severe gingivitis, although no definite oral lesion could be demonstrated.

When the patient was admitted to the University Hospital, the Kahn reaction of the blood was negative. Urinalysis showed no abnormality, and the blood count showed 65 per cent hemoglobin, 4,000,000 erythrocytes and 1,900 leukocytes, with 88 per cent polymorphonuclears, 1 per cent eosinophils and 18 per cent lymphocytes.

The patient was placed on a regimen consisting of application of calamine lotion to all cutaneous lesions, a high protein diet, with supplementary vitamin B_1 and frequent saline mouth washes. On the day after her first blood count another white cell count showed 2,100; about a week later the count was still only 3,300. However, about this time it was noted that the upper parts of her legs had become markedly involved by the same sort of eruption as she had on the upper part of her body. A tuberculin test at this time gave negative results, and she was given 2 grains (0.13 Gm.) of bismuth subsalicylate intramuscularly, and oral administration of quinine sulfate (0.32 Gm. three times a day) was started. While the new lesions were developing on the lower extremities, the original lesions faded markedly. About two weeks after administration of quinine was started, marked tinnitus and general malaise developed, and the white blood cell count reached about 2,500. Quinine was discontinued, but the malaise persisted, and she had marked elevations in temperature, as high as 105 F. During this time the condition of

the skin remained much the same. Administration of sulfanilamide was then started, 1 Gm. orally four times daily. She was given this drug for three days, after which a transfusion of 500 cc. of blood was employed. Great improvement in her general condition followed promptly, while her temperature steadily decreased to normal. Five days after the blood transfusion, her hemoglobin content was reported as 68 per cent; her white cell count had risen to 6,200. Concomitant with the improvement in her general condition, all of her cutaneous lesions faded steadily. The borders of the lesions, which had been definitely elevated, rapidly smoothed out. On Oct. 31, 1937, the patient was discharged, with instructions to return if necessary. On Jan. 5, 1938, there was a recurrence of a discrete macular eruption on the chin, the neck and the upper part of the chest.

NOTE.—The report from the University Hospital, Ann Arbor, Mich., is presented by permission of Dr. Udo J. Wile.

Case 8.—Cervical Adenitis and Erythema Induratum. Presented by DR. LOREN W. SHAFFER, Detroit, for DR. J. F. KILROY and DR. S. H. SAUTER, of the City Physician's Office, Detroit.

A. M. W., a well developed Negress aged 19, first noticed a swelling of the cervical glands in 1931 and has noticed lesions on the lower extremities for the past eight months. In 1930 a diagnosis of arrested tuberculosis was made and in 1934, a diagnosis of tuberculous adenitis. Roentgen therapy was advised at the latter date but declined.

The patient presents numerous hypertrophic scars on the right side of the neck, extending from the angle of the jaw to the chin. Active lesions under the chin, the size of a hickory nut, have been discharging until recently. There are three large plaquelike areas of induration on the legs. There is a lesion 2 by 3 inches (5 by 7.6 cm.) above the left internal malleolus, and two smaller areas are present on the exterior and the posterior surface of the right ankle. These have a rather doughy consistency and were recently lanced. The lesions are not painful.

Permission for biopsy was refused. A tuberculin test gave a 2 plus result on Dec. 3, 1937. Roentgenograms of the chest on Dec. 2, 1937, showed no abnormality. The Kahn test was negative on Nov. 26, 1937.

Case 9.—Tuberculosis Cutis. Presented by DR. THOMAS H. MILLER, Detroit.

M. J., a Negress aged 45, a housewife, born in the United States, complains of an eruption on the nose and the right ankle.

In February or March 1937 a painless indolent ulcer developed on the right ankle, just above the external malleolus. There had been no previous injury. After several weeks the ulcer healed spontaneously, but the borders were raised and appeared warty.

In June 1937 a "cold sore" developed on the upper lip and a "pimple" on the tip of the nose. The "cold sore" healed, but the "pimple" has continued to develop up to the present time.

The patient was first seen on Nov. 5, 1937, when she presented similar lesions on the left naris and the right ankle. These lesions consisted of pea-sized and smaller nodules, raised and slightly pinker than the surrounding skin. They were firm but not shotty when palpated. The surface of the lesions was verrucous, with a seropurulent exudate which crusted on drying. No apple-jelly nodules were seen under diascopic pressure.

The patient has received fractional roentgen treatment and four injections of sodium gold thiosulfate. There has been some improvement in the condition.

The Kahn test was negative on two occasions. Histologic examination of a specimen showed a picture resembling blastomycosis, but no organisms were observed. The condition is probably an example of atypical cutaneous tuberculosis, which is seen particularly in Negroes.

Case 10.—A Case for Diagnosis (Rosacea-like Tuberculid of Lewandowsky?). Presented by DR. LOREN W. SHAFFER, Detroit, for DR. J. F. KILROY and DR. S. H. SAUTER, of the City Physician's Office, Detroit.

Z. M., a white woman aged 54, first noticed an eruption involving the cheeks and the forehead two years ago. At first the lesions were few and not especially conspicuous and caused no symptoms. There has been a gradual and progressive increase in the number of lesions, which have remained of about the same character as at first. The lesions appear to be accentuated by excitement, by physical activity and by hot applications. Telangiectasia is not conspicuous. There has been no tuberculosis in the family. The patient's husband had syphilis, and she states that she had intravenous treatment for syphilis. Repeated Kahn tests have been negative since 1934, as has the serologic reaction of the spinal fluid.

The eruption is confined to the forehead and the cheeks, which are dotted by numerous papules varying in size from that of a pinhead to that of a millet. Some are level with the skin, while others are slightly elevated. They vary from bluish to brownish red. There are no active pustules and little scarring. Diascopy shows a faint apple-jelly-colored central punctum to persist in the individual papule. No necrosis or notable scarring is present.

The histologic report stated: "A rather marked, sharply defined infiltration was present beneath the epidermis in the uppor portion of the corium. The epidermis was slightly flattened and atrophic. The infiltration contained numerous epithelioid cells, a number of giant cells of the Langhans type and a dense infiltration of lymphocytes about the periphery. There was no central necrosis."

The Kahn test, urinalysis and serologic tests showed no abnormality. A tuberculin test with 0.1 cc. of tuberculin with 1 : 10,000 dilution gave positive results.

Case 11.—Lichen Scrofulosorum. Presented by DR. LOREN W. SHAFFER, Detroit, for DR. J. F. KILROY and DR. S. H. SAUTER, of the City Physician's Office, Detroit.

E. K., a well developed Negro aged 23 months, presents lesions of more than a year's duration on the trunk. These lesions have appeared progressively and have enlarged peripherally, clearing in the center, with depigmentation, and many have undergone complete involution. Others are in various stages of evolution. A new lesion is now developing on the upper part of the right arm. There has been no tuberculosis in the family.

The child presents grouped pinhead-sized lichenoid papules in discoid and annular patches on the trunk. Each papule is covered by a slight scale. The papules tend to undergo involution in the center, leaving an area of depigmentation with moderate scaling, surrounded by a ring of papules at the border. The patches vary in size from small groups of a few papules to irregular circinate areas the size of a silver dollar, but most of them are about the size of a 25 cent piece.

The biopsy specimen was not satisfactory, as the pathologic changes were apparently missed in cutting.

Scrapings showed no fungi. The Kahn test was negative. Roentgenograms of the chest on Jan. 6, 1938, showed a slight enlargement of the left hilar shadow, with the suggestion of the shadow of an enlarged node in the left axilla. The tuberculin test gave negative results. The blood count showed 94 per cent hemoglobin, a color index of 0.79, 3,760,000 erythrocytes and 8,750 leukocytes, with 48 per cent polymorphonuclears and 52 per cent lymphocytes.

Case 12.—Sarcoid, with Lesions on the Arms Resembling Papulonecrotic Tuberculid. Presented by DR. ROBERT C. JAMIESON, Detroit.

A. L., a white woman aged 39, unmarried, presents small and large reddish intracutaneous nodules on the fingers, the arms and the face (the lip, the nose and the forehead). The family and the past history are essentially irrelevant.

The lesions began in 1927 and progressed in number and extent until the patient was first observed in 1930. The patient is of the pituitary (acromegaloid) type, and weighs 208 pounds (94 Kg.).

When first examined she had reddish nodules varying in size from that of a pea to that of a small nut; these were both intracutaneous and subcutaneous. Those on the arms tended to have dry, necrotic centers and left atrophic scars when they healed. The larger nodular lesions were bluish red, and the smaller papular lesions on the arms presented the typical clinical appearance of papulonecrotic tuberculid. The nodular lesions were widespread, being present on the face, the fingers, the hands, the neck, the trunk and the buttocks. The smaller lesions appeared only on the arms.

The Wassermann reaction was negative. The blood count was normal. The basal metabolic rate was +11 per cent. Urinalysis showed a 2 plus reaction for sugar. Chemical analysis of the blood showed 100 mg. of sugar and 171 mg. of cholesterol per hundred cubic centimeters. Biopsy of a lesion on the arm in 1929 showed chronic tuberculosis of a lesion on the finger, in 1937, sarcoid and of a lesion on the shoulder in 1934, sarcoid.

A roentgenogram of the pituitary body showed that the sella was smaller than normal.

Gold therapy was employed from 1929 to 1931, and there was involution of the small lesions. Roentgen and radium therapy and excision were used on scattered individual lesions.

Case 31.—A Case for Diagnosis. Presented by DR. ROBERT C. JAMIESON, Detroit.

J. R., a white man aged 33 years, manager of a bank, complains of brownish red rounded plaques on various parts of the body. The family and past history are irrelevant. The lesions have developed slowly during the past three or four years, the first lesions appearing on the outer aspect of the lower third of the left leg. Other lesions appeared from time to time as brownish red intracutaneous nodules of varying size, with no subjective symptoms.

On the left leg is the first plaque that appeared. This is now about 8 cm. in diameter. The surface is smooth and shiny and slightly elevated above the level of the skin. There was, apparently, involvement of the subcutaneous tissue, but some involution has taken place in the past two months. On the other parts of the leg, on the arms and on the face similar, smaller lesions are following the same course. All are cutaneous or intracutaneous and reddish brown. None has undergone ulceration or spontaneous involution.

Physical examination and laboratory tests showed no abnormality. The histologic examination showed the lesions to be of embryonal cell type, lymphoblastomatous or sarcomatous. The condition has improved during the past three months, owing to administration of solution of potassium arsenite.

DISCUSSION

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: When I went over these cases, it became apparent that a number of them could be grouped to advantage. Unfortunately, they were not serially numbered in groups at the presentation, and I have taken it on myself to regroup some of them, in order to hasten discussion and to bring related cases together as nearly as possible. It is entirely probable that a great many of the members will not agree with my grouping. However, it is obvious that discussion in an assembly of this size is impossible if one member wants to discuss case 7 with case 10 and another to discuss case 25 with case 33. Hence, in spite of the fact that the members may not agree with my grouping, I should like to run over it for a moment. I have taken 12 cases, representing, I should say, possible and probable tuberculosis and sarcoid, and have made them group 1. Now these cases as I have grouped them—and please understand that the members are entirely at liberty to disagree in discussion—are cases 1-6, 8-12

and 31. I have grouped 3 cases of obvious disturbance of pigmentation, cases 14, 15 and 16, together. Because they represent various forms of localized or generalized scleroderma or scleredema, cases 17, 20 and 21 have been put together. Because I should like calcinosis to come next, I have put cases 30 and 35 in the next group. Then it seems to me that 2 cases (13 and 25), while possibly not instances of true poikiloderma, at least show poikiloderma-like changes in the skin. It seems to me that those should reasonably be discussed together. In 2 other cases (28 and 29) there is obvious resemblance. They are cases of necrobiosis. For the remainder, it seems to me, there is no advantage in an attempt at grouping, and they will be taken as nearly in numerical order as possible. The discussion on the first group will be opened by Dr. Michelson.

Dr. H. E. Michelson, Minneapolis: I intend merely to discuss the cases as they impressed me, and I do not wish to open a controversy. Many of the members may have slightly different conceptions regarding the skin and tuberculosis and we must abide by what is generally accepted and not by the particular opinion of any one of us. I feel that the clinical diagnosis must always be established first. If, then, the microscopic diagnosis fits in well with the clinical conception, well and good, and if the allergic state further confirms the clinician's opinion, so much the better. There is no international classification at the present time, and as far as I am concerned one may accept any classification one wishes. There really is no sensible basis for classification except the clinical picture, and under clinical picture I mean to include the morphologic picture and the course. In certain cases tuberculosis of the skin is so clearcut that there is no room for controversy, but the borderline type allows one to draw one's own conclusions.

Case 1, I think, is an instance of lupus vulgaris, with much lymphatic stasis giving the lesion the appearance of lupus tumidus and it is interesting to note that the roentgenograms of the chest were reported as showing no sign of tuberculosis. I do not think that the average examination of the chest, even by roentgen ray, furnishes sufficient evidence to justify excluding tuberculosis, because in the sanatorium the clinicians often find tuberculosis when it has been missed by other physicians.

There are many facts in case 2 that would have to be ascertained before a decision would be possible.

Case 3 presents a difficult problem. Dr. Pinkus kindly pointed out to me what looked like a tubercle bacillus, and the microscopic picture resembles sarcoid. This patient may have a nodular form of tuberculosis with a sarcoid structure.

Case 4 was presented as one of sarcoid. The diagnosis probably was made from a microscopic section, but to me the condition is clearly lupus vulgaris. The classic nodules are present; the color is characteristic, and diascopic examination confirms that diagnosis. In cases of lupus vulgaris it is common to find a sarcoid-like structure, and this case emphasizes again that clinical diagnosis must come first.

Case 5, I believe, is another instance of lupus vulgaris. The disease is of mild plane type, and the structure microscopically resembled sarcoid.

Regarding case 6: It is common to find erythema induratum and colliquative tuberculosis combined. There are certain well known combinations, and that is one of them. I want to emphasize that tuberculous adenitis is common in the aged.

Case 9 I diagnosed as one of hypertrophic lupus vulgaris.

My diagnosis in case 10 is lupus miliaris disseminatus faciei. I think that a decision will have to be reached about the diagnosis of rosacea-like tuberculid. Several forms of tuberculosis of the face with a rosacea-like distribution are diagnosed as that condition, and I doubt if there is a particular form which can be called rosacea-like tuberculid and nothing else. The decision must be made on the type and the size of the lesion, the duration, the allergic background and the microscopic picture.

For case 11 lichen scrofulosorum is a possibility, but there is not enough evidence to make me willing to commit myself.

Case 12 is most unusual. I should like to see an active lesion before making a final decision, but the scarring, the distribution and the waves of activity all point to papulonecrotic tuberculid.

DR. I. J. ARNSSON, Buffalo: Of this group I should like to discuss cases 2, 4, 9 and 10.

In case 2 the eyebrows are absent, and there is a certain leonine expression about the face. It would be advisable to look for Hansen's bacilli, since no neurologic examination has been made. The diagnosis of leprosy cannot be excluded without neurologic examination.

Case 4 I believe to be one of lupus vulgaris. Although, as Dr. Michelson said, the histologic picture was that of sarcoid, the clinical picture is entirely characteristic of lupus vulgaris.

The histologic picture in case 9 is that of syphilis. Nodular syphilid should be considered.

Case 10 is one of rosacea-like tuberculid and not of lupus follicularis disseminatus. In the latter disease necrosis and miliary cysts would appear in the histologic picture.

DR. HOWARD J. PARKHURST, Toledo, Ohio: On case 4 I agree with the previous speakers, who consider the lesions on the buttocks apparently typical of lupus vulgaris. The other lesions—the nodules on the forehead, on the back, on the leg and on the sole—would not have impressed them that way. The clinical and the histologic appearance and the course of these other nodules were characteristic of Boeck's sarcoid; the change in the tuberculin test, from negative at the height of the activity of these nodules to strongly positive when they subsided, would agree with that diagnosis.

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich.: I should like to add some remarks on case 9, because such a case offers difficulties in the differential diagnosis between tuberculosis and syphilis. The histologic picture alone will not decide the question, and antisyphilitic treatment sometimes produces some improvement in lupus. Besides the involvement of the nose, there is an involvement of the palate. The configuration of this oral lesion, especially, speaks strongly in favor of syphilis. On the other hand, there are many yellow tuberculous-appearing nodules. I believe that in such a case bacteriologic investigation by acid-fast stain, culture and the inoculation of a guinea pig will best decide the question.

DR. RICHARD S. WEISS, St. Louis: There seems to me no question as to the diagnosis in this case. It appears to be a typical instance of the disseminate form of lupus erythematosus. The cutaneous lesions were apparently precipitated by sunlight, a not uncommon occurrence. The patient does not present all the symptoms associated with what might be called the composite picture of lupus erythematosus disseminatus.

The disseminate types may be classified as follows: 1. The early type described by M. F. Engman Jr. (ARCH. DERMAT. & SYPH. **35**:685 [April] 1937), which usually occurs in hyperactive women of the society type or in extremely hard working, high pressure young people, who work under severe strain and spend half the night having a good time. The cutaneous manifestations in these patients include faint erythematous phenomena, transient urticaria and symptoms of erythema multiforme. There is a tendency to leukopenia in these cases when the disease begins to develop into the typical form; usually there are prodomal attacks of illness of some kind, with complaints of fever, lassitude and anorexia. 2. The typical acute exanthematic type. Usually there is a history of numerous griplike attacks, or of attacks of tonsillitis or sore throat, together with bouts of fever of more or less septic type. The disease is frequently associated with arthritis or arthralgia. Serositis, manifested especially as pleuritis or pericarditis, is common, and occasionally peritonitis occurs. The eruption is erythematous and urticarial or resembles that of erythema multiforme. However—and this seems to me important—the eruption may not be pronounced. In fact, it may be almost absent. Changes in the blood include definite leukopenia and a slight shift to the left in

the Schilling count, much more marked when terminal infection develops. The leukopenia may be relative and vary somewhat with the fever. Degenerative processes follow in various organs, characteristically in the kidneys, where there is so-called wire loop degeneration. 3. The type preceded by thrombocytopenic purpura. It is necessary in a discussion of lupus erythematosus disseminatus to inquire into the relation of the disease to the Libman-Sacks syndrome, in which symptoms suggesting lupus erythematosus are associated with nonbacterial endocarditis, to scleroderma of certain types and to sclerema adultorum of Buschke.

For the purpose of stimulating discussion I suggest that the incidence of lupus erythematosus disseminatus is increasing; that the disease is due to a definite infection; that there is a possibility that the infection is by virus and that the same virus may in different persons produce dissimilar phenomena; that the virus is, so to speak, getting more and more acclimated to the human habitat—or, in other words, its virulence is increasing; that the increased incidence is real and not a matter of better diagnosis, and that the disease can occur with little or no eruption.

Dr. Edward F. Corson, Philadelphia: Regarding case 6 alone, I have no disagreement with the diagnosis. This appears to be an open and shut case of lupus erythematosus disseminatus, with the frequently accompanying leukopenia and vitiligo. Together with Dr. J. B. Ludy, of Philadelphia, I have been attempting to establish the possibility that a mineral poison, a metallic substance is a factor, along with the bacterial toxin which seems to be responsible in many cases. We have been studying the effect of saturnism acting through the production of hematoporphyrin, which we have found in a comparatively large percentage of cases of acute and subacute lupus erythematosus, and the appearance of lesions of lupus following exposure to sunlight. This girl lives on a farm. Her knowledge of the metallic parts of the home pumping system is not such as to make us at all sure that lead piping is present. However, there is the possibility that in the spraying of fruit trees the spray is blown on roofs which are used for the collection of water for the cistern and that an element in the spray is responsible. We have incinerated biopsy plugs from the skin in numerous instances of lupus erythematosus and almost without exception have found the lead lines to be decidedly evident on spectroscopic examination. Since reading our paper in Atlantic City, N. J., last June (Arch. Dermat. & Syph. **37**:403 [March] 1938), we have had a number of additional cases of lupus erythematosus, especially in persons working in an electric storage battery plant, where they are constantly exposed to lead.

Dr. Theodore Cornbleet, Chicago: During the last three months I have been observing a case of lupus erythematosus combined with motor changes of the nasopharynx. This is the second case of this syndrome which has come to my attention in two years. I had the benefit of Dr. O. S. Ormsby's observations as a check in my first case. Such paralyses as occurred in both patients lend color to the view that metallic intoxication may be the basis of lupus erythematosus. It seems to me, however, that metallic intoxication cannot account for all that occurs in this disease. I believe that, until more information is found, the infectious theory best accounts for everything in the picture. Dr. Weiss's point about the leukopenia is worth while. Utilizing this isolated association, I have administered pentnucleotide to patients with lupus erythematosus. I am sorry to say that this agent was without any benefit. I agree with Dr. Weiss in his belief that the incidence of lupus erythematosus of the disseminated type is on the increase. One must look in the medical wards if some of the patients are not to be missed. I have found as many in the nondermatologic wards of the Cook County Hospital as in those especially for patients with diseases of the skin.

Dr. Samuel Ayres Jr., Los Angeles: In glancing over the history of this case, I saw no reference to investigation for the presence of focal infection. My feeling is that in this particular type of lupus erythematosus, where there is evi-

dence of dissemination and of photosensitivity, the first point of attack should be focal infection. This patient has definite enlargement of the cervical glands on both sides.

DR. H. N. COLE, Cleveland: By carefully questioning this patient, I learned that he had had a local process on his face—lupus erythematosus—that he was given heavy metal therapy and that after this the present generalized eruption developed, which I think could easily be due to bismuth.

GROUP 2

Case 14.—A Case for Diagnosis (Blue Nevus? Argyria?). Presented by DR. ARTHUR E. SCHILLER, DR. CLYDE K. HASLEY and DR. WILLIAM G. SAUNDERS, Detroit.

R. W., a boy aged 12 years, complains of a bluish black discoloration confined to the external border of the right eye by its bony orbit. The color is deeper on the upper portion and extends downward over the lid to within a short distance of the margin. There is no fading when pressure is applied. Inferiorly the color is not so dense and does not extend over the entire lower lid. There is no discoloration of the conjunctiva.

He had a series of infections of the throat, the ears and the sinuses, followed by a mastoid operation in 1931. He had a tonsillectomy in 1929, after an attack of scarlet fever. At present he has a rheumatic type of cardiac disease.

When he was 2 years old, after an injury, the eye and the lid were swollen and ecchymosed. The discoloration has remained about the same since that time. The patient states, however, that the discoloration is more noticeable after severe exercise, but this did not prove to be so when exercise was attempted. He has no sight in the left eye.

Roentgenograms of the chest show hilar adenopathy, with possible tuberculosis of the type seen in childhood. The Mantoux test gave negative results. Biopsy was not made.

Case 15.—Argyria. Presented by DR. FRANK STILES, Lansing, Mich.

J. T., an unmarried white woman aged 21, presents a dark brown pigmentation which involves both upper and lower lids. The pigmentation appears reticulated and assumes a vascular distribution.

She had a sinal infection and an operation for the removal of bone from the nose four years ago. This was followed by treatment with mild protein silver on alternate days, more or less continuously for two years. Mild protein silver was used twice in the conjunctiva. The pigmentation developed during the treatment and has increased since. No drug containing metal or a dye has been used locally since. Biopsy was not made.

Case 16.—A Case for Diagnosis. Presented by DR. ROBERT C. JAMIESON, Detroit.

A. M., a white woman aged 21, presents pigmentation of the frontal area and of the cheeks surrounding the eyes. She says that pigmentation of the scleras has been present since she was an infant. The present type of pigmentation was first noticed when she was 14 and has gradually increased since then. The patient has never been sick. She menstruated first at 13. No history of the use of drops of any kind in the eyes was obtained. Ophthalmoscopic examination showed no abnormality.

On the forehead, the cheeks below the eyes, the temporal areas and the eyelids is an increasing amount of blue-black pigmentation, but no elevation of the affected areas. On the central portion of the face are brownish pigmented lesions of the lentigo type. The lower portion of the scleras shows the same blue-black pigmentation.

DISCUSSION

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I suspect that considerable controversy might arise here. However, one of the members from Chicago has recently been interested in metallic pigmentation, and I think probably in at least 1 of these cases the condition comes under that heading. Consequently, I am going to ask Dr. Mitchell to open the discussion of these cases and tell the members something about this recent work on pigmentation with heavy metals.

DR. JAMES H. MITCHELL, Chicago: I was much interested in these 3 cases. The girl with the lesions on the eyelid called to mind the girl Dr. Oliver presented last year at the Chicago meeting, who had had hot applications on the lids for conjunctivitis (ARCH. DERM. & SYPH. **34**:730 [Oct.] 1936). The question at that time was whether the condition was *ab igne* retiform dilatation of the vessels (livedo) or lichen planus. The present case has some of the characteristics of both, and it may be an instance of lichen planus. There are definite papules, but no lesions elsewhere which suggest lichen planus.

Case 16 is extraordinary, in my opinion. There are two kinds of discoloration—brown pigment on the cheek and bluish discoloration which, for all I know, is a blue nevus or a nevus of some sort. I am inclined to believe that the bluish pigmentation is not due to silver, and to the same opinion in case 14. There was no record in either case of the use of silver. The absence of pigmentation of the scleras in the boy would be against argyria.

I was asked by Dr. Keim to present a little work (not original) that I did as the result of observing a case which was presented (ARCH. DERM. & SYPH. **36**:917 [Oct.] 1937) last January at the Chicago meeting (ARCH. DERM. & SYPH. **36**:639 [Sept.] 1937) as an instance of possible gold pigmentation. The article of Alvarex Cascos (Étude comparative des pigmentations métalliques: Argyrose et chrysose, *Ann. de dermat. et syph.* **7**:751 [Aug.] 1936) suggested to me a possible means of demonstrating the presence of the metal. I secured a section and with the aid of this simple technic was able to satisfy myself at least that silver and not gold was present. The technic makes use of the dark field. The stain used in the section is of no importance. Silver is deposited in fine granules, especially in the capsule of the coil gland; mercury is found in strands in the connective tissue, and gold is found in large clumps. The particles of gold are of irregular size and shape. Some of the particles may be large, whereas all the particles of silver are small.

I regret that it was impossible to get a section in which gold was present. Dr. Richard Weiss, of St. Louis, kindly sent sections but these showed no metal. Dr. William Sweeney of the City of Chicago Municipal Tuberculosis Sanitarium, Chicago, wrote to various friends in Europe, but as yet I have not been able to get a section showing gold pigmentation. If any one has a section, I should be much obliged to be given the opportunity of studying it.

(Dr. Mitchell's discussion was followed by a lantern demonstration.)

DR. S. W. BECKER, Chicago: I can vouch for the work so ably presented by Dr. Mitchell, because E. B. Ritchie and I (Argyria from Silver Arsphenamine, ARCH. DERMAT. & SYPH. **23**:773 [April] 1931; Argyria Following Excessive Use of Silver Arsphenamine, *J. A. M. A.* **97**:389 [Aug. 8] 1931) some years ago used the dark field method, as recommended by R. Habermann (Ueber Argyria cutis nach Silbersalvarsan und den Wert der Leuchtbildmethode E. Hoffmanns für ihren Nachweis, *Dermat. Ztschr.* **40**:65 [Jan.] 1924). Some beautiful colored illustrations accompanied Habermann's article. Dr. Ritchie and I used the method to confirm the diagnosis of argyria in cases in which excessive amounts of silver arsphenamine had been administered. Dr. Keim told me that some patients with possible argyria would be presented; when I first saw patient 12, I noticed that her face was rather dark and without committing myself asked her whether she had noticed any change in her color; she replied that her face was becoming purplish. She stated that she had received an injection of a gold compound weekly for three years, so here may be the case of chrysiasis which Dr. Mitchell is looking for.

The 3 patients exhibiting pigmentation form an interesting group. Such bluish discoloration as that about the right eye in case 14 is produced only when there is a certain amount of pigment deep down in the cutis. It is seen in tattoo, either deliberate or resulting from injury associated with grinding in of road dust or carbon. The lesion followed an injury accompanied with swelling of the eye. I have never seen this type of pigment from persistence of hemosiderin deep in the tissues. Hemosiderosis, seen frequently on the legs, presents a rather brownish pigmentation. The boy does not show any browning of the conjunctivas, which is the first sign of argyria, so I question the possibility of argyria.

Case 15 impressed me the same as it did Dr. Mitchell, as being an instance of retiform postinflammatory melanosis of the eyelids, such as is seen following the application of heat, or melanosis calorica; there is no browning of the conjunctivas to indicate argyria.

In case 16 pigmented scleras have been present since birth, which I think places the condition definitely in the class of blue nevus. The melanoblasts were deep enough in the connective tissue to give the bluish black color. The lesion has evidently extended, as they sometimes do, and the patient now has a blue nevus over a great deal of the forehead. Some brown ephelis-like lesions are present on the upper portion of the cheeks. While I do not believe that they are freckles, they certainly differ from the bluish lesions on the forehead and seem to indicate some pigmentary anomaly, the pigment being largely in the epidermis and producing a brownish color. There is no browning of the conjunctivas, which eliminates argyria as a possibility.

Dr. Samuel M. Peck, New York: I agree with Dr. Becker. I do not believe that in any of the 3 cases the condition is argyria. Although the boy stated that the peculiar bluish lesion around the eye followed trauma, I have never been able to produce any permanent blueness or discoloration from experimental purpura. However, it is common to find long-standing pigmentation due to deposits of blood pigment around old ulcers on the legs. The human animal is one of the few pigment-producing mammals who are capable of producing melanin as part of the regenerative process of the melanoblasts when light is completely absent. That is why marked pigmentation is often present around the rectum. One of the most frequent irritants tending to produce melanin formation is heat. For the production of more or less permanent pigmentation with melanin, large amounts of the substance have to be deposited in the tissues, most of it free but some in fixed tissue histiocytes. I think, therefore, that in this case of peculiar reticulated pigmentation on the eyelid there is postinflammatory pigmentation.

In case 16 the pigmentation on the face and on the conjunctivas, present since birth, probably is nevus. It must be borne in mind that almost permanent self tattooing following inflammatory processes is not infrequent. Dr. Isadore Rosen, of New York, presented a case at the meeting of the American Dermatological Association in New York in 1935 in which a white man practically turned into a Negro due to remarkable melanin formation following a chronic dermatitis. Histologic examination showed melanin in large masses lying free in the tissues.

Dr. Fred D. Weidman, Philadelphia: I wish to discuss case 14, that of the young man with the bluish pigmentation which seems, according to the two previous discussions, to be a nevus. I feel that it is a nevus, because the bluish discoloration of the conjunctiva is so irregularly distributed. If it were argyria, I should expect it to be more diffuse and uniformly distributed. That, though, is not the reason I stood up. It is because with any nevic condition of the skin there may be other associated and related nevic conditions of the ectodermal derivatives of the animal. I am thinking particularly of the cerebrospinal nervous system. Some of the members must recall E. W. Netherton's paper (Extensive Pigmented Nevus Associated with Primary Melanoblastosis of Leptomeninges of Brain and Spinal Cord, Arch. Dermat. & Syph. **33**:238 [Feb.] 1936) describing a young girl with extensive cutaneous nevus (and I think a bathing trunk distribution) who

exhibited at necropsy a melanotic sarcomatous change in the cerebrospinal nervous system. For this reason, in a case of this sort attempts should be made by both clinical neurologic examination and laboratory methods to discover nervous involvement. Perhaps actual melanin or, if not that, melanogen may be demonstrated in the cerebrospinal fluid.

GROUP 3

Case 17.—Morphea (Unilateral Distribution). Presented by DR. EUGENE A. HAND, Ann Arbor, Mich.

E. N., a married white woman aged 25, has lesions on the right leg, the hands, the arms and the shoulder.

At the age of 13, after her first menstrual period, the patient noticed a stiffening of the skin over the anterior portion of the thigh. This lesion healed eventually, with scarring. The condition spread to the right arm and shoulder. On the arm it has been chiefly localized in the ulnar region. The condition was much worse during each pregnancy. The treatment has consisted chiefly of thyroid medication.

The basal metabolic rate has always been within normal limits. The laboratory reports were essentially irrelevant.

Case 20.—Scleredema Adultorum (Buschke). Presented by DR. UDO J. WILE and DR. GEORGE H. BELOTE, Ann Arbor, Mich.

G. S., a girl aged 15, has had suppurative tuberculous cervical lymphadenitis for four years. This has been irradiated nine times and incised once. She has had a moist cough for a month. There have been no symptoms referable to the skin, with the possible exception of an inability to open the mouth widely, which she attributes to the soft tissue swelling.

Examination shows a pale healthy-looking afebrile girl with marked cervical adenitis and a peculiar distinctive hardness and stiffness of the skin. This is most marked on the back of the neck and the shoulders and extends by continuity from this region over the scalp, the face (sparing the eyelids), the arms and hands (sparing the fingers and the palms), the chest (to the costal margins) and the back (to the buttocks). The involved skin is moderately pale, smooth, shiny, devoid of wrinkles and furrows and too stiff to permit deep indentation with the finger. Such indentation, if produced, does not persist. The forehead does not wrinkle on forced upward gaze; lateral rotation of the head is limited, and there is moderate masking of facial expression. The skin cannot be picked up in folds. Pigmentation, secretion and sensation are not, apparently, disturbed.

Urinalysis showed no sugar or albumin. Examination of the blood showed 75 per cent hemoglobin (Sahli), 4,500,000 erythrocytes and 4,800 leukocytes, of which 68 per cent were polymorphonuclears, 31 per cent lymphocytes and 1 per cent eosimophils. The Kahn reaction was negative. A roentgenogram of the chest showed no abnormality. The basal metabolic rate was —18 and —11 per cent, respectively, on two occasions. The protein content of the serum was 8.5 mg. per hundred cubic centimeters, and the albumin-globulin ratio, 0.06. Over two months the albumin content of the serum rose from 3.1 to 3.9 mg., while the globulin content fell from 5.4 to 3.9 mg. The cholesterol content of the blood was 176 mg. per hundred cubic centimeters.

Histologic examination of an excised portion of an involved lymph gland showed the characteristic picture of tuberculosis. Examination of adjacent skin showed the epidermis and the subpapillary layer of the corium to be normal with a scanty nondescript round cell infiltration about some of the vessels. In the deeper layers of the corium the collagen bundles were strikingly enlarged and separated, leaving numerous clear spaces in the section. No other changes were observed.

The patient received small doses of thyroid extract, which have produced marked improvement in the past two weeks.

Case 21.—Scleroderma. Presented by Dr. Arthur E. Schiller, Dr. Clyde K. Hasley and Dr. William G. Saunders, Detroit.

C. D., a girl aged 5 years, presents stiffening of the skin of the left leg. The family and past history are immaterial.

The condition started on the outer surface of the left leg about one and one-half years ago. The mother states that the leg felt more firm, but there was no change in color until December 1936, when a brownish pigmentation was seen on the leg; after this waxy-looking patches appeared through the entire area and became confluent, forming a large indurated patch.

The patient was first seen in March 1937. At this time the area of scleroderma extended from the knee to the crest of the ilium laterally and anteriorly to Poupart's ligament. The skin, besides being waxy, was brownish, and the left leg was thinner than the right. Erythema doses of ultraviolet radiation were given to the affected area, and thyroid was administered internally. There was improvement in the areas involved, but during the treatment there was extension to the level of the nipple on the left side. Recently a small morpheaform patch was found on the shoulder. Involution in the last-formed areas was faster than in the early areas.

All laboratory tests made gave negative results. Permission for biopsy was refused.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: Two of the cases shown are undoubtedly instances of localized scleroderma, about which there is no controversy. I am glad that the members of this group could see the third patient but sorry that she could not have been seen some months ago. At present she has undergone a most extraordinary change for the better. When I first saw this young woman and it was suggested to me that she might have so-called scleredema adultorum of Buschke, I could not agree with the diagnosis. It seemed to me that she presented a picture in no way different from that seen in the edematous stage of generalized scleroderma. The face, as it is today, was masklike. She could not roll back the skin of the forehead, and that over the neck, the upper parts of the arms, the chest and the back was distinctly infiltrated and had the lardaceous feel of early scleroderma.

However, it was pointed out to me by members of my staff, who disagreed with me, that the extremities were not involved, particularly that the hands and the feet showed no infiltration, and that the course of the disease had been somewhat different from that of ordinary scleroderma. A diagnosis of scleredema adultorum, as originally described by Buschke and more recently by Sweitzer, was established; it was predicted that rapid improvement would occur, which now has turned out to be the case.

The patient now presents skin which for the most part is much more nearly normal than it was weeks ago, and it seems not unlikely that she will completely recover, as patients with scleredema adultorum do. An additional point of interest is a definite focus of tuberculosis in the neck, a biopsy of which showed an active lesion. However, cases have been described in which scleredema was accompanied with or preceded by some septic focus. In no other case, so far as I know, has tuberculosis been an accompanying finding. I do not offer this as evidence of cause and effect and believe that the cause of this entity is still obscure.

Dr. Paul A. O'Leary, Rochester, Minn.: I think the groups of scleredema, generalized edematous scleroderma and dermatomyositis have a great deal in common. I feel that clinical distinction between these diseases is not possible, particularly at their onset. I agree with the point that Dr. Wile mentioned, that scleredema is frequently self limited, running its course in approximately six months, disappearing and leaving no residue. Dermatomyositis has many features in common with scleredema, particularly at its onset. However, the histologic features are the ones that I should like to discuss. Generalized edematous scleroderma at

the onset is apparently cutaneous and subcutaneous, and frequently muscular, whereas dermatomyositis is fundamentally muscular. The relationship between cutaneous and muscular disease has been more or less ignored, a fact evidenced by the impossibility of finding in dermatologic literature any definite information about acute muscular infections. I think the other point worthy of comment is the course which these diseases pursue. In some cases of dermatomyositis the course is limited, as in scleredema, while in other cases the process will go on to death, or to calcinosis, as evidenced by the patient presented today. What has interested me particularly in the few cases of acute scleredema and acute dermatomyositis that I have been able to study is that I have been able to satisfy myself at least that there is a definite infectious process. However, my success in demonstrating this infection has been limited to cases of early involvement, because in dermatomyositis after the muscular atrophy becomes marked the infectious organism, usually a streptococcus, cannot be demonstrated.

GROUP 4

Case 30.—Calcinosis Circumscripta. Presented by Dr. George Van Rhee, Dr. Claude W. Behn, Dr. John Hamlin Besancon and Dr. J. H. Cobane, Detroit.

S. W., a white woman aged 25, American, presents lesions on the left elbow which followed an injury seventeen years ago, and some on the left knee which followed an injury fifteen years ago. Some lesions on the right hand began ten years ago. Since then lesions have developed on the left thumb. There has been no injury, but the lesions are affected by cold.

The lesions on the left knee and elbow and on the terminal phalanges of the right thumb and index and middle fingers and the left thumb are plaquelike. The plaques are studded with whitish blue and yellow nodules the size of a pea. Some of the nodules are inflamed and slightly tender and seem to have undergone necrosis. The nodules on the fingers and the thumb feel boardlike and atrophic and are slightly tender. They resemble sclerodactylia. The plaques on the left elbow and the left knee were removed surgically, and there was no recurrence.

A blood count showed 92 per cent hemoglobin, 4,410,000 erythrocytes, and 8,900 leukocytes, with 77 per cent polymorphonuclears, 15 per cent lymphocytes, and 8 per cent monocytes; there were 69 per cent segmented forms. The sugar content of the blood was 100 mg. per hundred cubic centimeters, the cholesterol content, 158 mg., the calcium content 8.8 mg. and the phosphorus content 3.3 mg. The Kahn test was negative. Roentgenograms showed deposits of calcium.

Dr. S. W. Becker examined and reported on the biopsy specimen from the left knee as follows: "The epidermis was markedly thickened over the center of the section and there was a suggestion of the opening of a sebaceous cyst. The material was decalcified a little too long to retain the basophilic properties of the calcium, and when it was received I noticed that the lower surface of the tissue showed considerable loose material which suggested cystic content. There was no bone formation in this material, although I am sure that there was bone formation in the section sent me before. I, therefore, make a diagnosis of dermal calcinosis, with the suggestion that the dermatoses may have taken place in an epidermoid or sebaceous cyst, although there was little evidence of a cyst wall. The condition did not appear to be calcified scleroderma."

Case 35.—Poikiloderma (with Calcinosis Universalis Due to Dermatomyositis Progressiva). Presented by Dr. Franz Blumenthal, Ann Arbor, Mich., and Dr. H. Pinkus, Eloise, Mich.

A. G., a white boy aged 19, a student, first noticed stiffening of the back about June 1931. Lassitude, increasing weakness, loss in weight and difficulty in bending to tie his shoelaces soon followed. Stiffness soon extended to the hips and the knees. At the outset there were hard, "stonelike" nodes in the groins. In the next two years progressive ankylosis of the elbows appeared, with wasting of the

muscles of the upper extremities. About a year after the onset an egg-shaped swelling appeared in the left axilla and broke down, exuding a "plaster-like" material. Similar processes occurred in the right axilla three years ago. In December 1935 the neurologic and the dermatologic services of the University Hospital at Ann Arbor, Mich., made a diagnosis of neurodermatomyositis ossificans progressiva. On Sept. 30, 1937, the patient was admitted to the Grace Hospital, Detroit, because he had severe dorsal pain, aggravated by motion and was bedridden; the skin was tender, and ulcers developed at points of contact. The remaining personal history and the family history are noncontributory.

Examination reveals a thin, emaciated, bedridden young man whose upper extremities are in flexion. There are marked oral sepsis, hypertrophic tonsils and pharyngeal inflammation. The blood pressure is 90 systolic and 65 diastolic. The skin in toto is thin and shiny and in places shows increased and decreased pigmentation and telangiectasia, giving the skin a spotted aspect, especially at the sides of the neck and about the eyes, the abdomen and the groin. On the bony prominences the skin is reddened. The skin is not thickened, but is shiny and shows changes in color similar to those following roentgen irradiation. Some points of pressure at the elbows and the sacrum appear like decubiti with calcium-like concretions. The abdomen, the groins and the upper parts of the thighs have a nonadherent skin with firm, plaquelike masses in the subcutaneous tissue and muscles. The nails are unchanged. In contrast to its condition in scleroderma, the skin is movable. On the scalp are changes similar to those on the body, with several small erosive lesions. The growth of hair is normal. The entire clinical picture gives the impression of diffuse atrophic cutaneous changes with poikiloderma.

The Kline exclusion test was negative. On Nov. 11, 1935, the calcium content of the serum was 10.6 mg. per hundred cubic centimeters of blood, on Oct. 1, 1937, 9.6 mg. and on Oct. 28, 1937, 7.2 mg.; the phosphorus content was 4.2 and 2.8 mg., respectively, on the latter two dates. Roentgen examination of the entire body showed multiple deposits of calcium in the soft tissues, indicating generalized interstitial calcinosis. There was no actual destruction of bone.

Biopsy on Jan. 3, 1935, by Dr. C. V. Weller showed interstitial myositis with fibrosis. On Jan. 19, 1935, a specimen showed marked atrophy with chronic interstitial myositis.

NOTE—This patient was presented by Dr. Udo J. Wile at the meeting in Ann Arbor, Mich., of the Detroit Dermatological Society in 1936.

DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: One thing that the term calcinosis denotes is the presence of lime in the skin. After that, though, the picture varies, a wide variety of circumstances possibly causing the deposition, and owing to the failure of dermatologists to appreciate that fact, considerable confusion exists in respect to the term calcinosis. From the general pathologic standpoint, the abnormal presence of lime in the skin is nothing more or less than calcareous infiltration. After that should be recognized the various circumstances with which it may appear. The most frequent is the presence of necrotic or necrobiotic foci, as, for example, old infarcts in the walls of arteries or scars in the skin. A comparatively rare associated phenomenon is abnormality of the parathyroid secretion, and rarest of all is calcareous metastasis. As to the last, during destruction of bone, e. g., suppurative osteomyelitis, the calcareous material may be carried by the blood stream and deposited in certain parts of the body. It is infiltrated in those parts whose "secretions" have a low *p*H—in ordinary terms, a high secretion of acid—for example, the stomach (hydrochloric acid), the kidney (uric acid) and the lung (carbon dioxide). I do not know of any instance of cutaneous involvement in this last class.

With these items in mind, how do cases 30 and 35 appear? In my opinion both are examples of calcareous infiltration of necrobiotic foci. In the first case, which has been exhaustively studied and beautifully illustrated by roentgenograms,

I found much necrobiotic material in the sections. The occasion for that necrobiosis I do not know, but I should say that the patients should be studied along the same lines as patients with xanthoma tuberosum. The condition should be studied apart from the secondary infiltrative phase, which may becloud the situation, just as in xanthoma. An attempt should be made to eliminate the yellow, xanthomatous features that preoccupy the observer and thereafter to determine some underlying and already established clinical dermatosis, just as the attempt is made to understand the fundamental processes concerned. Perhaps the same idea might be carried into the realm of calcification of the skin.

I was gratified when Dr. P. A. O'Leary anticipated me just a little. I agree that case 35 is probably one of dermatomyositis, or, as Osler called it, deep scleroderma. In the foci of necrobiosis in connection with the dermatomyositis there has been a deposition of lime salt.

In case 30, that of the young woman with atrophy of three fingers, Dr. Polk pointed out to me that the symptoms correspond to the distribution of the median nerve. The primary processes are, I imagine, trophic. Perhaps the fundamental processes are neurologic, and in connection with those atrophied and devitalized tissues with a low p_H there has been deposition of lime salts. I should suggest examination for cervical ribs. In this case gout might, for a moment, be considered, but the histologic sections do not bear out that possibility. In the sections there are necrobiotic foci again, and there is evidence of calcification. Dr. Becker has studied the sections and was not able to see ossification. That, however, involves only academic difference. Bony metaplasia, which ordinarily rates as ossification, takes place commonly in necrobiotic foci, whether they are calcified or not.

GROUP 5

Case 13.—A Case for Diagnosis. Presented by Dr. George Van Rhee, Dr. J. H. Cobane, Dr. Claude W. Behn and Dr. John Hamlin Besancon, Detroit.

A. M., a white woman aged 67, presents general hyperpigmentation varying from light to dark brown, which began about eight years ago. At that time there was marked itching and dryness of the skin on both wrists, which gradually spread to the forearms and arms. In the last four years she has gained from 90 to 100 pounds (40.8 to 45.4 Kg.). The pigmentation is most marked in the cubital spaces, the inner surfaces of the upper arms, the axilla, the cheeks and the temples. There is mild dermatitis with scaling on the flexor surfaces of the arms, from the wrists to the axillas.

One brother died of tuberculosis, one of diabetes and one of cardiac disease.

Roentgenograms revealed cholelithiasis. Otherwise the entire gastrointestinal tract was normal. The gynecologic examination revealed no evidence of infection by Trichomonas. There was no evidence of malignant growth.

The blood count showed 4,250,000 erythrocytes and 8,900 leukocytes, with 5 per cent stabpolymorphonuclears, 42 per cent segmented forms, 38 per cent lymphocytes, 10 per cent monocytes and 5 per cent eosinophils. Urinalysis showed a 2 plus reaction for sugar. The value for blood sugar in the sugar tolerance test at two and one-half hours was 142 mg., the chloride content (determined as sodium chloride) 429 mg., and the cholesterol content, 207 mg., per hundred cubic centimeters; the icterus index was 5. The van den Bergh test gave a negative result. The Kahn test was negative. The blood pressure was 160 systolic and 100 diastolic. The presence of hematoporphyrin is to be reported on later.

Case 25.—A Case for Diagnosis. Presented by Dr. William G. Wander, Detroit.

L. S., a white woman aged 55, states that lesions appeared successively on the thighs, the buttocks, the abdomen, the breasts, the arms and the back. Her family and past history are essentially irrelevant. She had a normal menopause at 52.

The present condition started two years ago on the inner surface of the right knee. She first noticed redness, itching and at times a burning sensation in this area. From this original area the lesions have spread to the aforementioned areas. They first appear as small areas of infiltrated dermatitis, and the itching and burning are most marked at this time. The lesions spread marginally and coalesce, when they are covered with fine flaky scales; later the spots become macular and atrophic. The distribution is strikingly symmetric. Physical examination showed no abnormality.

The urinalysis showed no albumin or sugar. The blood count was within normal limits. The Wassermann and the Kahn test were negative. The basal metabolic rate was + 9 per cent.

The treatment consisted only of local palliative applications.

DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: Poikiloderma is one of the most difficult diseases to understand and to define clearly. While the symptom complex is not sufficiently characteristic to allow placing the condition in any given case with certainty, there is a cutaneous symptom complex that fits Jacobi's original description of poikiloderma atrophicans vasculare. The most striking feature of this disease is the presence, as a rule, of patches of variable size in which there are pigmentation, atrophy and telangiectasia. These patches closely resemble healed radiodermatitis. My first patient presented a number of these characteristic areas. The fundamental symptoms are telangiectasia, hyperpigmentation, depigmentation and atrophy. The lesions are roughly symmetric and may occur on any part of the cutaneous surface and on the buccal mucosa. The disease dvelops insidiously and progresses slowly but continuously over a long period. Occasionally generalized lupus erythematosus is closely simulated. Telangiectasia and leukoplakia-like lesions may occur on the buccal mucosa. Poikiloderma-like symptoms occur in association with a number of cutaneous diseases such as mycosis fungoides. Poikilodermatomyositis indicates the cutaneous picture of poikiloderma in association with muscular sclerosis. The condition in case 35 probably belongs in that class. Scleropoikiloderma indicates the same cutaneous picture in association with sclerodactylia.

The subject became more confused when Civatte recorded a condition under the title "reticulated pigmentary poikiloderma of the face and neck" (*Ann. de dermat. et syph.* **4**:605, (1923). This disease occurs chiefly in women and is characterized by pigment and atrophic erythroderma arranged in a network. The lesions consist of macules and reddish brown slightly infiltrated patches. In addition, areas of pigmentation and superficial atrophy occur. By diascopic pressure telangiectasia may be demonstrated in the patches.

A similar disease was described by Kerl from the Riehl clinic under the title "Riehl's melanosis" (*Arch. f. Dermat. & Syph.* **130**:436, 1921). In Kerl's cases, in addition to the characteristic reticulated, pigmented and atrophic lesions of the face and neck, hyperkeratotic lesions were noted at times in the scalp and on the trunk. Other war melanoses, such as those induced by tar or an impure petrolatum ointment, were excluded from the classification.

In 1926, in a clinic at Strasbourg, France, was presented an example of Riehl's melanosis which Civatte immediately recognized as identical with his reticulated pigmented poikiloderma (*Bull. Soc. franç. de dermat. et syph.* **36**:848, 1929). It is now generally conceded that these two reticular pigmented dermatoses represent a single entity and that they are in no way related to poikiloderma of Jacobi.

In regard to cases 25 and 13: In the former, a woman presents patches of slight redness, pigmentation, telangiectasia and atrophy, rather generally distributed over the cutaneous surface. There are no subjective sensations, and some of the patches suggest healed radiodermatitis. It is an instance of idiopathic atrophy which tentatively can be placed in Jacobi's class of poikiloderma. In case 13 the woman presents a rather general hyperpigmentation, on which hyperkeratotic lesions are present. The pigmentation of the face is diffuse and resembles

chloasma. There are reticular pigmentation on the sides of the neck and generalized pigmentation composed of small discrete lesions, some of which are keratotic. While I cannot definitely place the condition, it does suggest a melanosis of the Riehl and Civatte type. It is possible that the melanosis is symptomatic of an endocrine disturbance.

DR. HOWARD J. PARKHURST, Toledo, Ohio: I do not like to disagree, but the location of the patches in case 25 on the extensor surfaces of the arms and forearms and on the lower extremities suggests to me an early stage of acrodermatitis chronica atrophicans.

GROUP 6

Case 28.—Necrobiosis Lipoidica Diabeticorum. Presented by DR. ROBERT C. JAMIESON, Detroit.

M. M., a married Jewess aged 22, presents several large reddish yellow rounded areas, distributed chiefly on the lower third of each leg.

Her mother and a paternal aunt were diabetic. Four brothers and sisters are living and well. The patient has been married three years and has one child.

The first lesion appeared on the lower part of the left ankle as a red rounded slightly elevated plaque 2 cm. in diameter and progressed peripherally, developing a reddish, violaceous border and a yellow atrophic morphea-like center, with capillary telangiectasia. There was no definite ulceration at any time. The patient is obese and presents no other dermatoses.

On the right ankle there is a similar area, 4 to 6 cm. in diameter, with no ulceration and no gangrene. On the lower third of the left leg are three similar lesions presenting the same characteristics, and on the outer aspect of the upper third of the left leg is the most recent lesion.

The lesions have all gone through the same progressive changes. The patient has had diabetes for five years and has received some dietary regulation and insulin therapy. The biopsy in 1931 was reported as showing sarcoid; the one in 1933, tuberculosis. Urinalysis previously showed a 4 plus reaction for sugar.

In addition to administration of insulin and dietary therapy, ultraviolet treatment was used for long periods up to February 1937; this produced no change in the appearance of the lesions. Since that time the lesions have lost their original characteristics.

Case 29.—Necrobiosis, Without Diabetes. Presented by DR. UDO J. WILE and DR. GEORGE H. BELOTE, Ann Arbor, Mich.

A. A., a housewife aged 28, in good health, states that a lesion appeared over the left shin seven years ago and has gradually extended in spite of all treatment. Since that time two other similar lesions have appeared. There are no marked subjective symptoms. Physical examination showed no essential abnormality, except for slight enlargement of the liver and the spleen, noticed by one examiner.

The patient has been under observation since January 1937. Examinations at that time showed three lesions confined to the anterior surface of the upper third of the leg. The largest was a slightly elevated round plaque measuring approximately 1½ inches (3.8 cm.) in diameter with a definitely yellow center and surrounded by a violaceous halo several millimeters wide. The entire plaque had a glazed appearance with fine scaling, through which many telangiectatic vessels shone.

The last examination, in December 1937, after a trial of a carbohydrate-free diet, showed peripheral extension of the largest plaque, the characteristic coloring remaining unchanged. A new, slightly painful penny-sized nodule had appeared between the largest plaque and the adjacent smaller one, and 3 cm. above the right ankle a similar tender nodule had appeared. The overlying skin of these most recent nodules was slightly reddish.

The results of the microscopic examination were reported as follows: "In the subcutaneous tissues were perivascular infiltrations of lymphocytes and plasma

cells. There were epithelioid areas with and without multinucleate giant cells. Areas of necrosis were noted. The picture did not resemble sarcoid, and while it showed some suggestion of tuberculosis, it looked more like a toxic necrobiosis than anything else. The pathologist asked whether the areas showing the aforementioned changes were located over the sites where injections of insulin had been made. Fat stains showed numerous droplets deep in the corium."

Examination of the blood showed 4,760,000 erythrocytes, 7,150 leukocytes and 69 per cent hemoglobin. The differential count was essentially normal. The test of hepatic function (with bromsulfalein) showed normal retention. The carotenoid content of the blood was 0.165 mg. per hundred cubic centimeters. The total lipoids, 600 mg. and the cholesterol content 190 mg.

The dextrose tolerance test, performed in January 1937 and repeated in December 1937, gave the following values for blood sugar:

	January (mg. per 100 cc.)	December (mg. per 100 cc.)
During fasting	83	64
First hour	84	68
Second hour	65	65
Third hour	59	51

DISCUSSION

Dr. Marcus R. Caro, Chicago: In both cases the lesions are clinically typical of necrobiosis lipoidica diabeticorum. In case 29 there is a good deal of yellowish discoloration of the skin clinically, but under the microscope the sections stained with sudan III showed no lipoid infiltration of the collagen fibers, as one would ordinarily find in this disease, and a few lipoid droplets were scattered throughout the tissues. In case 28 there is available no section stained with sudan III, but the histologic changes with the other stains were characteristic of the disease.

I questioned the patients as to possible injuries of the legs preceding the onset of these lesions, but both stated they had had none. I cannot help feeling, however, that injury plays a role in the production of these lesions. They occur principally on the legs, and the legs are often subject to trauma so slight that the patient does not notice it. Dr. H. Rattner, of Chicago, has at present under observation a patient in whom there is a single lesion of necrobiosis lipoidica diabeticorum at a site that is being rubbed and pressed by a garter clip. The trauma in this case may be an etiologic factor.

I think it would be instructive if some one attempted to produce a lesion artificially, either by repeated friction or possibly by injecting a small amount of necrotizing substance under the normal skin in a patient, before bringing the hyperglycemia of the diabetes mellitus under control. It would be interesting to see whether in such patients the excess lipoids circulating in the blood would be deposited at the site of the injury to produce artificially a lesion of this type.

Dr. E. P. Zeisler, Chicago: These 2 cases illustrate the well known dermatologic adage that when one's attention is called to a condition one discovers cases. About a year and a half ago, in Boston, a group of cases were shown from Dr. E. P. Joslin's clinic, and Drs. H. E. Michelson and Carl Laymon of Minneapolis, have had a number of cases in their part of the country. The clinical features of these cases are so typical, with the firm nodular consistency of the lesions, and the changes in color so characteristic, with the violaceous border merging into the bluish red and reddish yellow and finally the yellow center, that, along with the histologic changes, there should be no difficulty in recognizing them. Now, in spite of the apparent absence of diabetes in 1 of the cases, it cannot be assumed that the patient never did have hyperglycemia. She has a normal amount of sugar in the blood at present, but it is possible that she had definite diabetes at one time, and I think the occurrence of these lesions is indicative of the presence of diabetes

at one time or another. A similar status obtains in cases of multiple xanthoma, which occasionally has an appearance and distribution similar to that of xanthoma diabeticorum without associated evidence that the sugar content of the blood is high.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I have had this case under observation for about a year, and I had hoped at this time to have the answer. Unfortunately, I have not. I think no one can dispute Dr. Zeisler's contention that this patient may have had diabetes at one time. On the other hand, I feel, from a limited experience, that spontaneous recovery, at least from severe diabetes, is probably rather rare. We have studied this patient rather carefully from the standpoint of diabetes. We had her in the ward a short time on an ordinary standard diet and then did the usual dextrose tolerance tests. As may be noted, that test resulted in a flat curve, a rather unusual curve, as a matter of fact, but on a low level.

In the last few months this problem of diabetes has again split wide open. Physicians not so long ago thought it was prettey well pegged on the basis of the pancreas. I am informed by authorities at present that this thesis is no longer held to be true; that there are at least two types of diabetes, and in one of them, perhaps, the pituitary is far more important than the pancreas. Clinically and microscopically, I think, there can be no doubt as to the diagnosis.

It seems to me that probably nothing can be gained by trying to group the remainder of the cases. They will be taken as nearly in order as possible.

MISCELLANEOUS CASES

Case 22.—Sporotrichosis. Presented by DR. F. R. MENAGH, Detroit.

M. C. C., a white woman aged 46, complains of lesions on the arms, which had their onset about the first of October 1937, when a small lesion appeared on the flexor surface of the left forearm, 7 cm. above the wrist. The patient had been handling gladiolus bulbs, some of which were infected with a fungous disease. There had been no contact with animals or with barberry bushes. About ten days or two weeks after the original lesion appeared, the patient noticed a deep, cord-like induration extending up the arm. Along this cord other lesions appeared, first on the forearms, then in the medial part of the left side of the elbow and finally on the medial aspect of the upper part of the arm.

A chain of seven lesions on the flexor and the medial aspect of the left arm covers an area 4 by 8 cm., each lesion being about 2 cm. in diameter. There are two more such lesions on the medial side of the elbow and one on the medial aspect of the upper part of the arm, midway between the elbow and the axilla. The lesions are deep-seated, appear granulomatous and are dusky red. They are not tender, and they discharge a thin serosanguineous pus. Two deep hard painless pea-sized lesions are felt in the subcutaneous tissue. No glands are palpable in the axillas.

Laboratory tests showed no abnormality except that organisms, which did not show on smears, appeared promptly when cultured on Sabouraud's medium. The growth appeared in four days and was moist, flat and gray at first. On the sixth day the center of the growth was dark. In hanging drop preparations the hyphae were seen to be branched and showed pear-shaped conidia occurring singly or in groups, either along the hyphae or as terminal groups. There has not been time to report on the results of animal inoculation. No biopsy was made.

DISCUSSION

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: Perhaps there are certain parts of the country or other countries where the disease is particularly common, but it is certainly seen rarely here.

DR. H. R. FOERSTER, Milwaukee: This case is worth discussing because of the infrequency with which sporotrichosis is seen. I do not believe there is any question about the diagnosis. The picture is typical, even though the lesions have

undergone considerable involution and the involution, under medication with potassium iodide, supports the original diagnosis. It is interesting to note that all the characteristic features of the majority of cases of sporotrichosis in the United States are present. In practically all cases the involvement has been of the localized lymphangitic type; it occurs most commonly on exposed parts, particularly the upper extremities, and there is usually a history, as in this case, of injury, with an inflammatory pyogenic type of lesion at the site, an interval of several weeks—in this instance four weeks—and then development in rapid sequence of cutaneous and subcutaneous nodules, and a thickened lymphatic cord extending up the forearm on the flexor surface to the axilla, without involvement of the axillary nodes. It is interesting that the woman is a florist. She handles bulbs of various flowers, chiefly gladioli; probably the organism was present in the material in which the bulbs were packed, in view of the fact that in many cases fertilizer used on shrubs or flowers and dampness have been factors. The cultures are interesting. Of the several tubes, one has the characteristic chocolate-brown culture of the American or lymphangitic type of sporotrichosis and one a white culture which bacteriologists would probably differentiate as another species, the type that produces European or disseminated sporotrichosis. It appears, however, that the same type of organism may, at different times, exhibit variations, particularly in color. The microscopic specimen, the hanging drop preparation, showed the characteristic pear-shaped spores. The clinical and the laboratory investigation of this case were well presented.

DR. E. W. NETHERTON, Cleveland: As Dr. Belote has already stated, this disease is rare in this section of the United States. During the past fifteen years I have observed only 1 case and this only recently. Dr. G. H. Curtis, my associate, reported this case (Disseminated, Subcutaneous, Gummatous, Ulcerative Sporotrichosis, *Cleveland Clin. Quart.* **5**:57 [Jan.] 1938), because of its rarity and because of the fact that it was of European type. Numerous cutaneous and subcutaneous nodules were disseminated over the body. These rapidly became abscesses. It is interesting that the diagnosis of sporotrichosis can be made only by culture or by animal inoculation.

Case 27. — Bourneville-Pringle's Disease. Presented by DR. FRANZ BLUMENTHAL, Ann Arbor, Mich., and DR. H. PINKUS, Eloise, Mich.

La V. B., a white woman aged 22, began at the age of 2 years to have "spasms" periodically. Attacks were more severe after the sixth year. She never learned to speak more than a few words, never ceased to wet her bed and had to be fed and dressed. Mental forces declined still more after the sixth year. She entered the Eloise Hospital, Eloise, Mich., in July 1933, owing to severe epileptiform attacks; at this time "acne" was noted on the face and the arms. Menstruation began at the age of 13; it was irregular and at times profuse. The patient has never been ill except for measles and whooping cough.

She is well developed and of small stature. There are lesions on the face and the right shoulder, in the lumbar region and scattered on the trunk. There are no lesions on the mucous membranes.

The facial lesions vary from skin-colored shiny papules the size of a pinpoint on the medial part of the forehead to pinhead-sized pink firm dome-shaped papules on the chin; they reach 2 or 3 mm. in diameter on the chin and the medial parts of the cheeks. The larger lesions are mostly flat, firm, of waxy appearance and skin colored or pink. Telangiectasia is visible in some instances. Lesions are particularly crowded in the nasolabial folds, where they become more prominent and even pedunculated. There are a small hairy pigmented nevus near the lower lip and scaly seborrheic patches at both ears.

There are several groups of crowded firm yellow-tinged papules on the right shoulder. The region over the lumbar spine is occupied by a firm and irregularly but sharply defined skin-colored plaque, approximately 8 by 10 cm. and elevated 2 mm., the surface of which resembles shagreen. Scattered over the trunk, par-

ticularly in a line near the left axillary fold, are several soft, more or less pedunculated tags and dome-shaped tumors up to 1 cm. in diameter.

Other pathologic observations include equinovarus on the right. The fingers can be hyperextended. The reflexes are hyperactive but not pathologic. The optic disks are a little pale and hazy, but no other changes of the eyegrounds are seen. The patient does not speak, and it is impossible to establish any contact with her. When left alone, she exhibits stereotypic playful movements of the fingers. Usually quiet, she at times pounds her head against the bed or the wall and bruises herself severely. She has epileptiform attacks at intervals of several weeks.

Roentgen examination shows no bony or articular changes of the hands, the spine, the pelvis or the skull. The sella is small. There is some calcification in the anterior horn of the right ventricle. The chest is normal. Pyelograms have not yet been made. Laboratory findings are irrelevant. The Kline exclusion test was negative.

Biopsy of sections from one of the papular lesions on the right shoulder showed lanugo follicles with slightly hypertrophic sebaceous glands and well developed arrector muscles. There was a spotty increase of finely fibrillar connective tissue in the papillary body, accompanied with disappearance of the elastic fibers from these spots.

Sections across the border of the large plaque on the back showed the papillae and the subpapillary layers to be increased to several times their normal width by coarse wavy strands of collagenous fibers, between which there were numerous small capillaries and apparently solid strands which contained but few fine elastic fibrils. The papillary body showed many fibroblasts and melanophores. The epidermis showed a thick horny layer, widened follicular openings and considerable lengthening of the rete pegs. The hair follicles and sweat glands had undergone atrophy and some had been destroyed by foreign body granulation tissue. The microscopic diagnosis was angiofibroma.

Case 32.—Kaposi's Sarcoma. Presented by DR. ARTHUR E. SCHILLER, DR. CLYDE K. HASLEY and DR. WILLIAM G. SAUNDERS, Detroit.

P. R., a white man aged 67, presented himself on July 23, 1937, complaining of cold feet and legs and numerous small, skin-colored and hemorrhagic growths on the dorsum of the feet. The skin has been discolored somewhat for approximately ten years, and recently he has had sharp pains in the areas of discoloration.

With the exception of the death of one brother, at 65 from tuberculosis, his family history is immaterial.

Except for the usual diseases of childhood, hemorrhoidectomy in 1937 and cholecystitis four years ago, his past history is irrelevant.

The skin is normal, except for that of the extremities, where he presents brownish red patches on the dorsal aspects, extending above the ankles. He has hard nodular pipestem arteries. There are no palpable masses or nodules anywhere. On both feet a number of ovoid hard papules and nodules, varying in size from that of a pinhead to that of a lentil, extend deeply into the skin. They vary from the color of skin to fawn and are firm to the touch. When first seen the patient presented a vascular tumor about 6 by 3 mm. and a number of smaller vascular tumors.

The blood pressure is 168 systolic and 78 diastolic. The Wassermann reaction was negative. Scrapings and cultures of material from lesions on the feet showed no fungi.

Two biopsy specimens were taken, one from the vascular and one from the nonvascular tumor. The pathologist's report follows: "Grossly the specimen includes two pieces of tissue which measure 6 by 3 by 2 mm. and 10 by 8 by 6 mm., respectively. The latter is a blood vessel filled with an old blood clot; the wall is 1 mm. thick. Microscopically, the specimen is an unencapsulated new growth composed of interlacing bundles of spindle cells. These are fibroblastic and exhibit moderate anaplasia. The diagnosis is angiosarcoma."

DISCUSSION

DR. CLARK W. FINNERUD, Chicago: The patient illustrates the almost invariable rule that in this disease there are extreme variations in clinical type of lesion; even vesicles and bullae may be present. Usually when the condition is well developed there can be little clinical question about the diagnosis. A finding almost constant, and usually not noticed, is the warty character of the skin of the sides of the dorsa of the toes.

Histologically an accurate diagnosis can usually be made, even in cases in which the clinical picture is the most atypical, because practically always, if a sizable piece of tissue is examined, several of the following elements may be observed: (1) definite angiosarcoma, (2) round cell sarcoma, (3) spindle cell sarcoma and (4) areas of capillary hemorrhage.

There is good evidence both that this disease is primarily a chronic inflammatory process which secondarily may become sarcomatous and, as J. Dörffel (Histogenesis of Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, ARCH. DERMAT. & SYPH. **26**:608 [Oct.] 1932) concluded, "is a disease of the reticulo-endothelial system, including a disturbance of the monocytogenetic function, which at times may terminate in true malignancy."

Although usually the metastatic growths occur chiefly in the gastrointestinal tract, in the lymph glands, the spleen, the pleura, the lungs and the muscles, in H. N. Cole and E. S. Crump's case (ARCH DERMAT. & SYPH. **1**:283 [March] 1920) leukemia developed.

Case 34.—A Case for Diagnosis. Presented by DR. LOREN W. SHAFFER, Detroit.

D. D., a white boy aged 14, has had attacks of "Vincent's angina" affecting the mouth and the lips for the past four years. He states that these attacks occur three or four times yearly but that he is not entirely well between attacks. No other member of the family, which includes three sisters, has had any similar condition. He was in the contagious hospital on three different occasions in 1936. Each time a diagnosis of Vincent's angina was made, evidently on the basis of positive smears.

The acute attacks start on the lips and spread quickly to the tongue and the rest of the mouth. At present an ulcerative process similar to that on the tongue involves the glans penis. He states that this was present during one previous attack. He has been treated for Vincent's angina by several physicians and dentists. He has had scarlet fever, chickenpox and measles.

His mother admits that he was given ex-lax wafers preceding this attack, and the boy states that he has frequently used a chewing gum laxative. He was advised to take a wafer of ex-lax as a therapeutic test on Jan. 12, 1938.

Examination shows an inflammatory reaction in the mouth and on the tongue, the gums and the lips. There is no active vesiculation or ulceration of the lips, but simply exfoliation in the process of involution. The buccal mucosa appears erythematous, with the suggestion of a slight membrane. The gums are not particularly involved. The tongue is the seat of the most marked inflammatory process. Numerous sloughing, serpiginous, superficial ulcers are present on the tongue, the rest of the surface being covered by an adherent thin grayish membrane. Deep ulceration is not present. An inflammatory process, with superficial ulceration similar to that present on the tongue is now present on the penis.

Three smears of material from the tongue showed no Vincent's organisms. The Kahn test was negative. The blood count showed 106 per cent hemoglobin, 3,840,000 erythrocytes and 14,700 leukocytes, with 73 per cent polymorphonuclears, 23 per cent lymphocytes and 4 per cent eosinophils.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I think this manifestation is one of many that can follow the ingestion of phenolphthalein. It is worth noting the close resemblance of the picture presented by this tongue to an old sclerosing

syphilid. I do not think I should have hazarded this diagnosis if I had not observed, within the last year or two, a case of serious ulceration of the tongue, ulceration of the lips, lesions on the penis—which this boy also had—and definite deep necrotic ulcers of the scrotum and thigh, in a patient who had taken phenolphthalein. The history of this boy's having taken ex-lax and the appearance of the tongue I think are presumptive evidence that this condition is a phenolphthalein eruption.

Case 18.—**Amyloidosis Cutis.** Presented by Dr. H. J. Parkhurst, Toledo, Ohio.

Case 24.—**Keratosis Follicularis (Darier's Disease).** Presented by Dr. F. R. Menagh, Detroit.

Case 26.—**Recurrent Fixed Erythema (Dermatitis Dysmenorrhoica?) in a Girl with Amenorrhea.** Presented by Dr. H. J. Parkhurst, Toledo, Ohio.

Case 36.—**Keloids Following Lesions of Rupial Secondary Syphilis.** Presented by Dr. Loren W. Shaffer, Detroit.

Case 7.—**A Case for Diagnosis.** Presented by Dr. Thomas H. Miller, Detroit.

Case 23.—**A Case for Diagnosis (Naevus Acneiformis Unilateralis?).** Presented by Dr. George B. Sexton, London, Canada (by invitation).

Case 33.—**Lichen Planus.** Presented by Dr. Arthur E. Schiller, Dr. Clyde K. Hasley and Dr. William G. Saunders, Detroit.

Case 38.—**A Case for Diagnosis (Pseudopelade? Lupus Erythematosus?).** Presented by Dr. Eugene A. Hand, Ann Arbor, Mich.

DETROIT DERMATOLOGICAL SOCIETY

George H. Belote, M.D., *President*

March 15, 1938

Thomas H. Miller, M.D., *Secretary*

Arthur E. Schiller, M.D., *Recorder*

A Case for Diagnosis. Presented by Dr. Thomas H. Miller.

L. H., a white woman aged 35, presents lesions on the face, one below the right eye and one on the left cheek. The family history is irrelevant.

In 1931 or 1932 a "growth" beneath the right eye was excised. The wound healed well, but after ten or twelve months scaling began. In July 1933 the patient presented a pea-sized ivory-colored scar with two milia at the upper border. The milia were removed, and the lesion was screened with lead and treated with 400 r of unfiltrated roentgen rays. It became smaller; no more milia formed, and there was no further change until June 1936. At this time a collection of sebaceous secretion (large comedos) appeared on the left cheek and at the upper border of the lesion beneath the right eye. Roentgen radiation (400 r) was given to each lesion. In October 1937 the lesion of the left cheek could not be seen, but the one beneath the right eye was scaly, bled easily and "pulsated" during the menstrual

period. Since that time it has not enlarged or changed in appearance. One or two small telangiectatic vessels have become visible at the upper border. At the site of the original lesion on the left cheek a small papular lesion containing a number of pinhead-sized yellowish points has developed.

DISCUSSION

DR. A. R. WOODBURNE, Grand Rapids, Mich.: I think that the type of sclerosis under the scar of excision is not particularly uncommon after irradiation. I do not believe, however, that I can recall ever seeing it after one caustic dose.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I do not believe that 400 r on each of two occasions in three years is of necessity a caustic dose.

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich.: The scar is absolutely white; there is no pigmentation or evidence of telangiectasia. I do not believe this form of scar can be produced by 400 r of roentgen radiation. At times one sees changes due to relatively small doses, but I do not believe this looks like a change due to roentgen rays.

DR. ARTHUR E. SCHILLER: The lesion on the left cheek interests me. The small raised nodules are distinctly yellowish, and I think the lesion might be xanthomatous.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I think the lesion on the left cheek is epitheliomatous. It is small but has a waxy shine. I think it is impossible to discuss intelligently the lesion under the eye, because nothing but a scar is left. I should call that an epithelioma also, possibly of the morphea type.

DR. THOMAS H. MILLER: Previous to my seeing this patient she had a growth excised in that location. About two years ago, when I first saw her, she had three rather large comedos and several milia at the upper border of the scar of excision. I was able to express the comedos and the milia. As they were increasing in number and size, I gave her the 400 r of roentgen radiation with the idea that perhaps it would stop the activity of the glands in that location; apparently the condition did clear for about three years but then appeared again.

As far as the condition on the left cheek is concerned, that cleared under the influence of roentgen rays for a couple of years and has been appearing again just within the last few weeks. I think the lesion on the left cheek may be a deposit of some colloid or xanthomatous substance. The lesion under the eye has enlarged in the last three years; so it must be something more than a scar. I took a tracing of it six months ago on cellophane, and it has not grown since then, but it is definitely larger than it was three years ago.

DR. H. PINKUS, Eloise, Mich.: Like Dr. Belote, I believe this lesion to be an epithelioma of the morphea type. It is not the same as scleroderma and is firmer than a scar would be.

DR. ROBERT C. JAMIESON: I have the same impression as Dr. Pinkus regarding the lesion under the eye. Toward the inner canthus there is a yellowish, morphea-like band, and directly under the eye is a small area which seems to be slightly reddened and scaly and has a rather firm attachment to the underlying structure, as though the lesion were undergoing epitheliomatous change. I should like to second Dr. Pinkus' suggestion that this is an epithelioma developing on morphea.

Early Recklinghausen's Disease. Presented by DR. ARTHUR E. SCHILLER.

E. L., a married white woman aged 38, presents a patch of depigmentation on the neck, which she states has been enlarging.

Examination discloses a number of café-au-lait patches of varying size covering the neck, the chest and the back. On the right side of the neck are two tumors the size of a glass pinhead. Along the lines of cleavage of the back are rather deeply placed firm ovoid areas, which do not appear above the surface of the skin.

DISCUSSION

DR. HARTHER L. KEIM: I suggest that the lesion is a unilateral pigmented nevus, which was brought out by the exposure to sunlight.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: It was presented as early Recklinghausen's disease. Is that diagnosis tenable?

DR. HOWARD J. PARKHURST, Toledo, Ohio: The pigmented area is not sharply demarcated in the midline, and there are café-au-lait pigmented patches on the other side. Other cases have been recorded in which these café-au-lait spots have occurred without the characteristic tumors.

Epidermolysis Bullosa. Presented by DR. ARTHUR E. SCHILLER.

D. C., a boy aged 3 years, since birth has had a bullous eruption on various portions of the skin when injured. The mother is a low grade feebleminded person with congenital syphilis. There are 3 sisters who have no cutaneous lesions. The father is well.

When the patient was born, a small lesion resembling a blister was present on the right instep. Within four hours similar lesions occurred all over the body; these have been present ever since, taking the form of large blebs, which apparently arise from the normal skin and contain sometimes clear and sometimes hemorrhagic fluid. The lesions heal slowly, with crusting. In the past year the new lesions have appeared at points of friction, as at the creases of the neck, the joints and the bony prominences.

The patient has a rather long history of hospitalization. He was at the Herman Kiefer Hospital for eight months, at the University Hospital, Ann Arbor, Mich., in 1936 and at the Children's Hospital after that. He was seen at the City of Detroit Receiving Hospital on Feb. 9, 1938, and at the Grace Hospital on Feb. 12, 1938.

Recklinghausen's Disease. Presented by DR. ARTHUR E. SCHILLER.

B. F., a white married woman aged 32, states that an inflammatory reaction appeared on the face and the neck after the application of certain medicaments to the face.

The patient is small; general physical examination showed no abnormality; she had dermatitis venenata of the face when first seen. However, examination at present shows café-au-lait patches covering the neck, the back, the chest and the abdomen, as well as the arms, and some small fibrous nodules along various portions of the body.

DISCUSSION

DR. G. WARREN HYDE: I think this patient shows the bony sclerosis that was talked about by Dr. Wise when he was here a couple of years ago, and I have 2 cases of Recklinghausen's disease in mind in which there is always definite sclerosis. I think sclerosis is something that should be looked for in all cases of Recklinghausen's disease.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: In some cases osseous cysts have been reported. I have studied a number of those cases roentgenographically, but I confess that I have never been able to find the cysts.

Lupus Erythematosus. Presented by DR. JOHN HAMLIN BESANCON.

E. M., a white woman aged 29, presents a rash on the face which has progressed slowly. She consulted the clinic when an itchy eruption developed under one arm. There were no subjective symptoms on the face.

She presents multiple small macules, with atrophic coalescing centers over the chin and the cheeks. The middle of each cheek is covered with normal skin.

There are no visible scales. Three weeks ago the patient had acute dermatitis in one axilla, which cleared under local therapy. (Apparently this had no connection with the present condition.)

The Wassermann reaction was negative. There was no improvement during quinine therapy. The patient is now on bismuth therapy, having had two injections.

DISCUSSION

DR. HOWARD J. PARKHURST, Toledo, Ohio: I do not agree with the presenter's diagnosis, and I have a substitute to offer: érythrose péribuccale pigmentaire (Brocq). It will be recalled that Drs. O. S. Ormsby and M. H. Ebert, of Chicago, presented a paper on that subject (Érythrose Péribuccale Pigmentaire de Brocq, ARCH. DERMAT. & SYPH. **23**:429 [MARCH] 1931) at the session of the American Medical Association in Detroit on June 26, 1930, and I was delegated to open the discussion. I committed the grievous error of confusing the condition with the perioral chloasma of virgins. These two dermatoses do not appear to be related.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I should say the only thing lacking is the pigmentation.

DR. FRANK STILES, Lansing, Mich.: The patient states that the lesions flare up before her menstrual period, which I believe is characteristic of the disease Dr. Parkhurst named. She says they get redder and brighter at that time.

Acute Lupus Erythematosus. Presented by DR. J. H. COBANE.

M. D., an unmarried white girl aged 19, presents an eruption on the face and the upper extremities.

Her paternal grandfather died of tuberculosis at the age of 40. She has had sore throat twice but no contagious disease.

Following a severe sunburn in 1936, an eruption appeared on the forehead and the cheeks, and there was a sparse eruption on the upper part of the trunk and the upper extremities a few months later. This cleared slightly during the winter of 1936. Lotions and ointments have not given any benefit. The eruption is asymptomatic. She had a tonsillectomy in December 1937 because of chronically septic tonsils and adenoids.

Examination shows her to be well nourished, with no general systemic clinical complaints. There has been no loss of weight, elevation of temperature or increase in pulse rate. On the forehead and on each side of the face are circumscribed solid patches of infiltrated erythematous, slightly scaling dermatitis, with minor pitting of follicles and signs of slight atrophy. The patches are sharply outlined.

In October 1937 an eruption began on the upper part of the trunk and the upper extremities, extending down to the wrists and consisting of erythematous, scaling and slightly atrophic dermatitis. Ultraviolet irradiation provokes erythema with scaling.

The Wassermann reaction was negative. A blood count showed 73 per cent hemoglobin, 3,600,000 red blood cells and 4,600 white blood cells, with 49 per cent polymorphonuclears, 39 per cent lymphocytes, 5 per cent monocytes and 7 per cent eosinophils. Urinalysis showed no abnormality. Permission for biopsy was refused.

The patient was treated with boric acid compresses and boric acid ointment, which produced mild benefit. Treatment by intramuscular injection of a bismuth preparation, oral administration of 5 grains (0.32 Gm.) of quinine three times a day and elimination of salt from the diet has recently been started.

DISCUSSION

DR. HARTHER L. KEIM: I agree with the diagnosis of lupus erythematosus, but I do not know about the acute part. The history goes back to the summer of 1936. The lesions are destructive—the larger ones on the cheek atrophic—and

resistant; they are associated with some tenacious scale. While the clinical picture is a bit atypical for the discoid variety of lupus erythematosus, I think this case should be classified with the group described by M. F. Engman Jr. (Early Acute Lupus Erythematosus (ARCH. DERMAT. & SYPH. **35**:685 [April] 1937). In this group of cases particularly young women were involved, most of them having leukopenia. (This patient had 4,000 white blood cells.) After Engman presented his paper, J. H. Stokes suggested that the condition may be a sequel to influenza or some of the common diseases of the upper part of the respiratory tract. Others suggested that the cause lies in the fact that young persons, particularly young women, are burning the candle at both ends, and all they need is good old-fashioned supportive therapy, including medication with drugs like cod liver oil.

DR. LOREN W. SHAFFER: I agree with the diagnosis, except that there is a possible question of classification. I think this condition should be classed as at least subacute lupus erythematosus, as the fact that the lesions on her forearms completely disappeared without any scarring or atrophy would seem to indicate. I suggest a trial of sulfanilamide in moderate doses. I think the experience in the use of sulfanilamide in the treatment of acute disseminated lupus erythematosus has been at least favorable, and that more experience is needed with that drug in cases of possible streptococcic manifestations on the skin.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I think the word "acute" should probably be stricken out, but otherwise I think the diagnosis is acceptable.

A Case for Diagnosis. Presented by DR. CLAUDE W. BEHN.

N. W., a Negress aged 35, entered the clinic on Nov. 7, 1936, complaining of pain and swelling in the joints of the hands, the arms, the feet and the legs, dating from June 1936. A gynecologic examination revealed no demonstrable infection. Bilateral salpingectomy had been performed seven years before, and four years later a second pelvic operation was performed, this producing an artificial menopause. A diagnosis of acute arthritis was made. A search for foci of infection revealed almost complete obstruction of the left nasal passage and a marked postnasal discharge. The tonsils were enlarged, with many infected crypts.

About the time of the onset of her arthritis several nodular, depigmented lesions developed over the extensor surfaces of the arms and the right hip. All the lesions showed rather marked telangiectasia. New lesions have continued to develop on the face and the trunk, and tenderness has become more pronounced. The surfaces of some of the older lesions became scleroderma-like. Roentgenograms of the joints showed typical arthritic changes. Roentgenograms of the chest revealed no abnormality. During the past two or three months a chain of nodules has developed along the veins of both upper and lower extremities and along the veins of the chest. During the summer tonsillectomy was performed, and since this operation the patient has had pronounced hoarseness.

Many blood counts have been made, the last one showing 86 per cent hemoglobin, 4,330,000 erythrocytes and 5,000 leukocytes, with 56 per cent polymorphonuclears, 17 per cent lymphocytes, 13 per cent monocytes and 5 per cent eosinophils. The urea nitrogen content of the blood was within normal limits. Urinalysis showed an occasional trace of albumin. The Wassermann reaction was 2 plus at one time but is negative at present. The basal metabolic rate was normal. The von Pirquet test gave negative results.

Treatment with doses of from 50 to 100 mg. of sodium gold thiosulfate and eight injections of neoarsphenamine with bismuth produced no response. An application of radium to the lesion on the nasal ala brought about a complete disappearance.

DISCUSSION

DR. A. R. WOODBURNE, Grand Rapids, Mich.: I should like to offer the diagnosis of periarteritis nodosa, a condition which is rather rarely seen with rheumatoid arthritis. It is a disease involving the blood vessels and producing a small

aneurysmal dilatation with granulomatous reactions, usually associated with fever. The course is ordinarily considerably shorter than in this case, but in reading the literature eight or ten years ago I found that the conditions may be chronic. I think the point in favor of this diagnosis as against that of ordinary rheumatic nodule, is that the lesions follow vascular distribution up and down the legs and the arms and are not particularly located around the joint.

DR. HARTHER L. KEIM: About fifteen years ago I was called to Jackson prison to see a Negro who had morphologically identical lesions in identical locations on the nose. A diagnosis of leprosy had been made, but microscopic examination of one of the nodules revealed the characteristic structure of lupus vulgaris. I have, accordingly, been particularly interested in this type of lesion since that time and have seen a number of examples which turned out to be tuberculosis. I should suggest that one of these nodules be examined microscopically. Whether the periarterial nodes are likewise of tuberculous origin I am not prepared to say. It is worth noting that the lesions on the external surfaces of the upper arms do not follow the course of the vascular tree and morphologically suggest the possibility of sarcoid.

DR. CLAUDE W. BEHN: This patient has been difficult to follow. As I remember, the first biopsy specimen was taken from the lesion on the nose, and there was no evidence of a tuberculous infection such as Dr. Keim suggested. However, I have always felt that the disease was tuberculosis, since all the types of treatment instituted have produced little or no improvement in the nodules. Many new nodules have developed since she was last seen, probably about nine months ago, and the nodules apparently followed the large vessels of the arms and the legs. A biopsy was done on one of the rather large but active lesions, and I will bring the section to the next meeting.

DR. GEORGE VAN RHEE: Possibly ten or fifteen years ago I showed a woman whose condition exactly duplicated this one. She is still living. A diagnosis of periarteritis nodosa was made. She had the same type of lesions at the alae of the nose and on the forehead, as well as nodules along the blood vessels. I presented the case as one of periarteritis nodosa, and Dr. P. F. Morse said patients with that condition die early. This patient is still living; her condition is much improved, with practically no treatment, and the nodules have gradually disappeared.

DR. LAWRENCE HAROLD BUTLER: I observed 2 cases in which the picture was similar to this in Buffalo; I studied them for several years, and the final diagnosis was avian sarcoid. One patient was sent to a leper's sanatorium. One dermatologic organization after another argued about them, and finally the disease was called avian tuberculosis, but it was very similar to this.

DR. LOREN W SHAFFER: I was much interested in this case from several angles, and I was particularly glad to be reminded of the possibility of periarteritis nodosa. I think the condition belongs in the sarcoid group, particularly on a basis of the lesions on the nose, the widespread nodules in the skin and one other thing that has not been mentioned, namely, the laryngitis that she has had for a number of months. I think it would be interesting to check the pathologic report on the tonsils and see if they showed typical benign lymphogranulomatosis of Schaumann. The fact that roentgen studies of the bones showed no sign of the disease does not mean that such signs will not appear, and Schaumann advised that to facilitate diagnosis examination of bone marrow removed with a punch be made.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Diagnosis of this disease is made at autopsy for the most part, and in the cases that have been reported in the literature the condition was discovered at autopsy. I know of 1 case in which there were repeated flares of the periarteritis nodosa, and the histologic diagnosis was characteristic. As far as I know the patient is still living.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: I think a further report on the microscopic picture of those nodules is essential.

Neurodermatitis Disseminata, with Cataract. Presented by DR. GEORGE VAN RHEE.

D. K., a white woman aged 22, entered the Harper Hospital in November 1930. She states that she has had eczema since she was 1 year of age. The eczema was of the moist type until 1937. There was no history of dermatoses in the family. She had otitis media with a discharge from the left ear for several years. Tonsillectomy was performed in 1933.

The examination at the time of admission revealed a generalized scaly papular dermatitis, with marked thickening of the skin, lichenification and increased pigmentation over the upper part of the body, involving the chest, the arms, the neck, the shoulders and the face. There was marked involvement of the cubital and the popliteal spaces.

Sensitization tests by the scratch method showed positive reactions to silk, redtop, dwarf ragweed and timothy. The basal metabolic rate was —7 per cent. The calcium and the inorganic phosphorus content of the blood were 10.6 and 2.5 mg. per hundred cubic centimeters. The dextrose tolerance test showed a trace of sugar in the urine after thirty and after sixty minutes; in the blood, a specimen taken during fasting, showed 114 mg.; one taken at thirty minutes, 125 mg. and one taken at sixty minutes, 95 mg. per hundred cubic centimeters. The blood count was normal.

The ophthalmologic examination on March 11, 1937, revealed postpolar cataract in the right eye; there were definite opacities in the left lens.

Treatment consisted of local applications, elimination diets and desensitization to silk and wool in increased doses; some benefit resulted.

Neurodermatitis Disseminata, with Cataract. Presented by DR. GEORGE VAN RHEE.

H. A., a white woman aged 26, entered the Harper Hospital in January 1936. She states that she has had eczema since she was about 6 years old. The eczema was of the moist type until 1933. There was no history of dermatoses in the family.

Examination at the time of admission revealed a generalized papular scaly dermatitis, with thickening of the skin, lichenification and increased pigmentation. The areas involved were the neck, the cubital and popliteal spaces and the thighs. There has been no apparent change. The patient has a nasal polyp and allergic rhinitis. The gastrointestinal examination showed limited pylorospasm; the gallbladder did not fill and there were indications of disturbance in its function.

Sensitization tests by the scratch method gave 2 plus reactions to wool, silk, and small ragweed and a 3 plus reaction to wheat. Since April 10, 1937, desensitization with wool and silk in increased strength has proved of some benefit.

On March 5, 1938, an ophthalmologic examination showed a matured cataract of the right eye; the fundus of the left eye was normal.

The basal metabolic rate was + 12 per cent. The sugar and the inorganic phosphorus content of the blood were 117 and 2.7 mg. per hundred cubic centimeters, respectively. The blood count was normal. In addition to the therapy previously mentioned, the patient has received local applications and an elimination diet.

DISCUSSION

DR. HOWARD J. PARKHURST, Toledo, Ohio: I am interested in such cases of cataract from a medicolegal standpoint. I have seen cataracts develop after prolonged irradiation, but in the first of these cases fractional weekly roentgen treatments were given, and in the second case there were no roentgen treatments. Various authors, I believe, have reported instances of atopic eczema in which cataract appeared without previous irradiation.

DR. HENRY A. BRUNSTING, Toledo, Ohio: The opportunity of observing these 2 cases was well worth my coming here. The association of cataract and atopic eczema is important. Ruby K. Daniel presented a paper on the subject before the Ophthalmologic section of the American Medical Association (Allergy and Cataracts, *J. A. M. A.* **105**:481 [Aug. 17] 1935); she reported 3 cases, and since then, approximately 25 patients with atopic eczema and associated cataracts have been seen at the Mayo Clinic. Some of them were reviewed by L. A. Brunsting (Atopic Dermatitis [Disseminated Neurodermatitis] of Young Adults: Analysis of Precipitating Factors in One Hundred and One Cases and Report of Ten Cases with Associated Juvenile Cataract, ARCH. DERMAT. & SYPH. **34**:935 [Dec.] 1936).

There are three schools of thought in reference to the production of these cataracts, one holding that it is probably associated with allergic phenomena, another that it is a result of roentgen or ultraviolet irradiation and the third that it is on the basis of a vitamin deficiency. For the possible allergic basis, it may be said that progress of the cataract has been seen in association with repeated flares of the eczema. Offsetting the theory of roentgenologic origin is the fact that 1 of these patients absolutely denied having had any roentgen irradiation. If roentgen rays would produce cataracts, I believe all dermatologists would see many more cataracts in patients with acne vulgaris treated with roentgen rays. Ophthalmologists are usually able to distinguish cataracts produced by roentgen ray from those due to allergic phenomena. While most of the patients have had dietary restrictions imposed on them, many have had vitamin therapy, but the cataracts have progressed nonetheless.

DR. FRANZ BLUMENTHAL, Ann Arbor, Mich.: The question of cataract following roentgen irradiation has led to a great many discussions. It is not easy to produce a cataract by roentgen irradiation, and when one does so it is with massive doses, much higher than are given in dermatologic treatment; so I do not believe that one can say that roentgen rays cause cataract. I agree with Dr. Parkhurst that it would be produced much more easily with ultraviolet rays, and one knows that persons who are exposed to ultraviolet rays have earlier cataracts than other persons. As to the questions of allergy and of vitamin deficiency, I believe the hypotheses are interesting, but I have not seen one single cataract in an allergic patient in Europe, and here they are rare; so I should like to suggest that not allergy but some other factor produces the cataract.

DR. ROBERT C. JAMIESON: I have had the unfortunate experience of seeing a cataract develop in a case of this type, and the endocrinologists have suggested one more possibility, that it is due to a disturbance of the thyroid secretion rather than to roentgen irradiation, a vitamin deficiency or any of the other causes suggested. Now, the question of the cause of atopic eczema is open to any suggestions, and endocrinologists seem to think that the thyroid—I will not say a deficiency but a thyroid imbalance—could explain the development of these cataracts.

Leiomyoma Cutis. Presented by DR. JOHN HAMLIN BESANCON.

M. G., a white boy aged 17, presents painful nodules on the right cheek. No member of his family has had a similar complaint.

There are many nodules, varying from the size of a pinhead to that of a marble. The larger ones are hard. When stimulated, the largest one contracts and turns white, and the patient experiences pain in that region.

The Wassermann reaction was negative. Histologic examination showed that, except for slight acanthosis at one end of the section, the epidermis was what may be regarded as normal. The corium was almost entirely occupied by broad interlacing trabeculae of involuntary muscle extending down to the level of the sebaceous glands. There was no evidence of circumscription (no capsule). The picture was typical for leiomyoma cutis.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2nd Ave., S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

J. J. McGovern, President, 4005 Dorchester St., Montreal.
F. L. Boulais, Secretary-Treasurer, 2061 St. Denis St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

J. Bedford Shelmire, Chairman, 1719 Pacific Ave., Dallas, Texas.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: St. Louis.

American Academy of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: St. Louis. Time: November 1938.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.

American Dermatological Association

Francis E. Senear, President, 55 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: Seigniory Club, Montebello, Ontario, Canada. Time: May 1939.

Society for Investigative Dermatology

George M. MacKee, President, 200 W. 59th St., New York.
S. M. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

---

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.

Mississippi Valley Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Francis McCauley, President, 31 Lincoln Pk., Newark.
Henri Abel, Secretary, 339 Union Ave., Elizabeth, N. J.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville, Fla.
Joseph A. Elliott, Secretary, Professional Bldg., Charlotte, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

M. Toulmin Gaines, Chairman, 404 Merchants National Bank Bldg., Mobile, Ala.
Clinton W. Lane, Secretary, 508 N. Grand Ave., St. Louis, Mo.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Norman N. Epstein, Chairman, 450 Sutter St., San Francisco.
Howard M. Engle, Secretary, 450 Sutter St., San Francisco.

Connecticut State Medical Society, Section on Dermatology

James D. Gold, Chairman, 839 Myrtle Ave., Bridgeport.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.

Florida Society of Dermatology and Syphilology

C. A. Andrews, Chairman, 706 Franklin St., Tampa.
Lauren Sompayrac, Secretary, 204 Laura St., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

George A. Dix, President, 6 Ashland St., Worcester.
J. Harper Blaisdell, Secretary, 45 Bay State Rd., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Mark Heiman, Chairman, 600 Medical Arts Bldg., Syracuse.
Timothy J. Riordan, Secretary, 136 E. 64th St., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

L. G. Beinhauer, Chairman, 5026 Jenkins Arcade Bldg., Pittsburgh.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.
Place: Scranton. Time: October 1938.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

George Van Rhee, Chairman, 10 Peterboro St., Detroit.
Ruth Herrick, Secretary, 26 Sheldon Ave., S. E., Grand Rapids.

MINNESOTA DERMATOLOGICAL SOCIETY

L. A. Brunsting, President, 102–2d Ave., S. W., Rochester.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Onis George Hazel, President, Osler Bldg., Oklahoma City.
Everett S. Lain, Secretary, Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

Everett R. Seale, President, 1215 Walker Ave., Houston.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Herman E. Kittredge, President, 1835 I St., N. W., Washington, D. C.
I. Louis Sandler, Secretary, 1835 I St., N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Samuel M. Peck, President, 125 E. 72d St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

David L. Satenstein, President, 57 W. 57th St., New York.
M. Edward Goebel, Secretary, 842 Union St., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Clarence H. Peachey, President, 197 S. Goodman St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Rudolph Ruedemann Jr., President, 256 State St., Albany.
Harry D. Parkhurst, Secretary-Treasurer, 264 Genesee St., Utica, N. Y.

CHICAGO DERMATOLOGICAL SOCIETY

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.
Place: Chicago. Time: Third Wednesday in January 1938.

CINCINNATI DERMATOLOGICAL SOCIETY

Leon Goldman, President, Doctors Bldg., Cincinnati.
George E. Clarke, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

John Gammel, President, 1020 Huron Rd., Cleveland.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

Detroit Dermatological Society

G. Warren Hyde, President, 2501 W. Grand Blvd., Detroit.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: May 1939.

Los Angeles Dermatological Society

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

Max Scheer, Chairman, 509 Madison Ave., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 450 Sherbrooke St., E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Eugene F. Traub, Chairman, 140 E. 54th St., New York.
Louis Tulipan, Secretary, 224 E. 17th St., New York.

New York Dermatological Society

J. Frank Fraser, President, 100 W. 59th St., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln.

Philadelphia Dermatological Society

Thomas Butterworth, Chairman, 411 Walnut St., Philadelphia.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

John C. Kerr, President, 62 14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary, Stambaugh Bldg., Youngstown, Ohio.

St. Louis Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Norman Epstein, President, 450 Sutter St., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland.
Place: San Francisco. Time: Third Friday of November 1937.